RECENT ADVANCES IN CARDIOLOGY

RECENT ADVANCES IN CARDIOLOGY

BY

TERENCE EAST
M.A., D.M., F.R.C.P.
Physician, and Physician-in-charge of Cardiological Department, King's College Hospital

AND

CURTIS BAIN
M.C., D.M., F.R.C.P.
Physician, Harrogate General Hospital
Physician-in-charge of Cardiographic Department
Royal Bath Hospital, Harrogate

Fourth Edition

With 27 Plates and 98 Text-figures



LONDON
J. & A. CHURCHILL L..D.
104 GLOUCESTER PLACE, W.1
1948

PREFACE

In preparing a fourth edition the opportunity has been taken to re-write the book entirely. Apart from the possibilities of improvement in arrangement and exposition, the considerable increase in knowledge during the last ten years makes this necessary.

As in former editions, we have tried first of all to keep in mind the needs of the general practitioner who wishes to keep abreast of this subject; as well as those of the student working for higher examinations, and the seeker after academic information. As we said in former prefaces, some matters which may now appear to be academic may become the commonplace of ordinary knowledge in a few years. In particular, emphasis is laid upon the early recognition of disorders, and upon their treatment.

As the title implies, a book of this sort aims at putting forward the newest information. In order to make this intelligible it has been necessary to include a survey of older material. The result is that a fairly comprehensive discussion of cardiovascular disease has been undertaken. But there has not been room for certain topics, and some are dealt with more shortly than in ordinary textbooks

The theme that runs through the book is the importance of the health and efficiency of the heart muscle. It is in respect of this that all the various lesions and conditions that may affect it are considered.

Congenital defects are considered first. They are classified, as far as may be, on a basis that refers to the stage in the development of the heart at which they [illegible] than the broad division into [illegible] the oxygenation of the bloo[illegible] may be for clinical purposes.

It is convenient to consider all the infections of the heart together; they have so much in common in their pathology and their effects on the function of the heart. Libman-Sack's disease comes in here as a well defined entity. These infective processes link up with pericardial disease; the special effects of the constricted sac on the circulation have been of great interest in the

1st Edition 1929
2nd ,, ... 1931
3rd ,, ... 1936
4th ,, ... 1948

Printed in Great Britain

whole does not merit this designation in relation to general medicine. Progress is rapid and knowledge is accruing fast, for the modern methods of investigation by intracardiac catheter of the output and venous pressure, has opened up a large field, the crops from which are hardly yet ripe for reaping. The possible rôle in the derangement of renal function in the pathogenesis of œdema and changes in blood volume are probably the first steps in something of considerable importance. But much is in the melting pot, and at this juncture one can only surmise the effect of many results and speculate on the lines of future advances. But there is no doubt that great progress is likely to be made in the next few years as all the available data are checked and correlated. The difficulty lies in their complexity and multiplicity. Even much of what was thought to be certain fact about the action of digitalis may require revision. From the better understanding of the treatment of heart failure comes further insight into its nature; the same applies to the circulation in general, and in particular to recent work on the retention of common salt in the pathogenesis of œdema.

Vascular diseases need a chapter, and there is a good deal new in the methods of investigation. Peripheral failure is still considered apart: this is at the moment convenient; much new work on wound shock has led to valuable information derived from war casualties. Of the medical side less is known: at a future date it should be possible to synthesize the phenomena of failure at the periphery with failure at the centre. Further progress is more likely to unite than divide.

In this edition cardiograms are for the most part considered with the topics to which they refer. In place of the older material there has been included a resumé of the modern ideas which seek to explain all the features of the curve by the mathematical expression of electrophysical changes. This is a step in the right direction, and will prove of absorbing interest; for the next step to pathological change is short. But the mathematics are abstruse and the physics complicated for the ordinary physician. This theoretical approach needs to be linked up with the practical results of the new methods of precordial leads and unipolar technique, so a chapter is devoted to these matters. There is no doubt that the use of multiple chest leads has added to the precision with which

last decade. Hypertension requires a long chapter. Much progress has been made in our knowledge of the effect that changes in the intrarenal circulation have on the circulation as a whole. How precisely these start is still a mystery; the treatment of the disease still awaits benefit from the new discoveries. Effective though lumbar sympathectomy may be in certain cases, it is really only palliative. The true cure, and more important, the prevention of this common disease, are still obscure. The special features of the cardiovascular derangements met with in thyrotoxicosis, anæmia and pregnancy, and vitamin deficiency are considered together. In the first thiouracil preparations have offered possibilities of the control of the activity of the gland; in the second, the peculiar circulatory changes have aroused further interest lately. Affections of the pulmonary circulation now have a special chapter. The incidence and effects of pulmonary infarction are the subject of an important advance in knowledge. There is no doubt that in the study of this part of the circulation great progress is to be expected.

Disease of the myocardium has a special chapter: this is a matter on which one may await greater correlation between morbid change and morbid function; there is still much to be learnt about causation.

It has been found convenient to consider together in the chapter on Tachycardia the circus movement and the ectopic disorders of rhythm. The trend of progress here is to link them all together, and the fact that they have so much in common in their causation and effect, helps this approach. Disorders of conduction and vagal slowing are also taken in one chapter, under the heading Bradycardia, although reduction in rate is not necessarily a feature. In these matters again, synthesis rather than schism seems to be the modern trend, "Entia non sunt multiplicanda praeter necessitatem." This principle of William of Occam has guided also our discussion of derangements of the coronary circulation, whether the deficiencies be transient or permanent, where the frequency of vasomotor disturbances is attracting more and more attention.

The account of the progress in the study of the hæmodynamics of heart failure has had very special attention. This is a true, actively growing point of knowledge; not that Cardiology as a

whole does not merit this designation in relation to general medicine. Progress is rapid and knowledge is accruing fast, for the modern methods of investigation by intracardiac catheter of the output and venous pressure, has opened up a large field, the crops from which are hardly yet ripe for reaping. The possible rôle in the derangement of renal function in the pathogenesis of œdema and changes in blood volume are probably the first steps in something of considerable importance. But much is in the melting pot, and at this juncture one can only surmise the effect of many results and speculate on the lines of future advances. But there is no doubt that great progress is likely to be made in the next few years as all the available data are checked and correlated. The difficulty lies in their complexity and multiplicity. Even much of what was thought to be certain fact about the action of digitalis may require revision. From the better understanding of the treatment of heart failure comes further insight into its nature; the same applies to the circulation in general, and in particular to recent work on the retention of common salt in the pathogenesis of œdema.

Vascular diseases need a chapter, and there is a good deal new in the methods of investigation. Peripheral failure is still considered apart: this is at the moment convenient; much new work on wound shock has led to valuable information derived from war casualties. Of the medical side less is known: at a future date it should be possible to synthesize the phenomena of failure at the periphery with failure at the centre. Further progress is more likely to unite than divide.

In this edition cardiograms are for the most part considered with the topics to which they refer. In place of the older material there has been included a resumé of the modern ideas which seek to explain all the features of the curve by the mathematical expression of electrophysical changes. This is a step in the right direction, and will prove of absorbing interest; for the next step to pathological change is short. But the mathematics are abstruse and the physics complicated for the ordinary physician. This theoretical approach needs to be linked up with the practical results of the new methods of precordial leads and unipolar technique, so a chapter is devoted to these matters. There is no doubt that the use of multiple chest leads has added to the precision with which

the diagnosis and localisation of infarcts can be achieved. It seems likely that still further correlation in the size and depth of the lesions will follow on a better understanding of the electrophysical changes which underlie abnormal curves. The examination of the heart by X-rays has been so much part of ordinary clinical procedure that no separate chapter is now assigned to it. The final chapter in other editions on the normal heart has been merged in the rest.

The inclusion of a very large amount of new work, in spite of rigorous pruning and excision, has made the book rather larger than before. There are many new plates and illustrations.

We hope that very up-to-date reviewers will bear in mind that the travail of authorship is prolonged in these days, and that the best part of two years elapses during the third stage between pen and publication. But knowledge advances nowadays *accelerando* and Achilles is hard put to it to overtake the tortoise. As we pointed out in our first preface nearly twenty years ago, what is recent and what is an advance is often conjectural; but in this space of time Cardiology has become established in a form and substance hardly to be thought of then.

We wish to thank Dr. J. W. Brown for permission to use illustrations from his book "Congenital Diseases of the Heart" (Staples Press) for Figs. 1 to 9, and Dr. Ashman and Dr. Byer for Figs. 94 and 95, which appeared in the *American Heart Journal*, and also Dr. Bayley for Figs. 96 to 98 from the same journal. Figs. 45 and 46, are reproduced from articles by one of us in the *Lancet*, and Figs. 17, 52, 68, 84, and Plate 20 have appeared in papers by us in the *British Heart Journal*.

To our publishers we offer our thanks for their help and courtesy.

TERENCE EAST,
Upper Wimpole Street,
London, W.1.

CURTIS BAIN,
Harrogate.

CONTENTS

CHAPTER I

CONGENITAL DISEASE OF THE HEART

During the last thirty years the embryology of congenital cardiac defects has been much investigated. Keith, in 1909, stressed the great importance of the imperfect involution of the bulbus cordis as a cause of several common lesions. Later on Spitzer (5) extended this theory and threw light on the effects of faulty rotation of the great vessels The analysis of a thousand cases by Maude Abbott (1) has correlated the clinical and pathological sides. Her clinical classification recognised three groups (1) the cyanotic, (2) the late cyanotic, (3) the acyanotic. We propose to adopt an embryological classification on the lines suggested by Dry (2). Not every lesion can be considered here. *The "Atlas" (1) and the excellent monograph by J. W. Brown (3)* gives a full account of all. On this latter we have drawn freely.

Classification

I Anomalies associated with septal formation

1. Cor biloculare.
2. Cor triloculare biatriatum.
3. Cor triloculare biventriculare.
4. Auricular septal defect.
5. Ventricular septal defects.
6. Persistent truncus arterosus (Aortic septal defects.)

II and III. Anomalies associated with torsion of the cardiac tube, and with the development or absorption of the bulbus cordis—

1. Transposition of the great vessels.
2. Tetrad of Fallot.
3. Eisenmenger complex.
4. Pulmonary stenosis (infundibular type)
5. Sub-aortic stenosis
6. Anomalies of aortic and pulmonary valves.

IV. Anomalies associated with development of the aortic arches :—

1. Persistent right aortic arch.
2. Double aortic arch.
3. Coarctation of the aorta.
4. Patent ductus arteriosus.
5. Anomalies of main branches.

V. Dextrocardia.

VI. Anomalies of coronary vessels

For full information the papers of Keith (4), Spitzer (5), Bremer (6), Pernkopf and Wirtinger (7), Lev and Saphir (8) and Walmsley's excellent account in Quain's Anatomy (9), should be consulted.

Development of the Human Heart

During its development the mammalian heart passes through various stages which resemble the hearts of lower animals: in each individual the history of the development in various species is recapitulated. The congenital malformations of the human heart recall structures found in the hearts of fishes, amphibians, reptiles and birds.

The process of development aims at establishing a pulmonary circulation "in parallel" with the systemic, instead of "in series." But they must communicate with each other, so the two are also "crossed." The heart begins as a fusion of two straight tubes placed on either side of the body, which are brought together as the primitive ventral cleft closes in. In the 3 mm. embryo this simple tube is already becoming divided into four chambers, the sinus venosus at the tail end, the auricle, the ventricle, and the bulbus cordis at the head end. This stage represents the heart of some fishes. As the primitive cardiac tube increases in length, between two fixed points, it becomes kinked or bent, or twisted upon itself. (Fig. 1.) The ventricle grows downwards and forwards, the auricle upwards and backwards. The ventricular part becomes a loop bent on itself in a v-shaped *manner, forming in the angle of* the loop the bulbo-ventricular groove. A twist

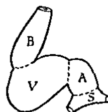


FIG. 1.

A. Auricle
B. Bulbus Cordis
S. Sinus Venosus
V. Ventricle.
(After Pichon)

also develops, clockwise at the ventricular end, anti-clockwise at the venous or caudal end. (Fig. 2.) It is suggested that the forces which bring about these changes are inherent growth, increase in length between fixed points, and the centrifugal force of the blood flowing round the curves and bends so produced (6).

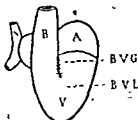


FIG 2

A Auricle
B Bulbus Cordis
B V G Bulbo ventricular groove
B V L Bulbo-ventricular loop.
S Sinus Venosus
V Ventricle
(After Pichon)

Division of Truncus and Bulbus. In order to develop the two circulations in parallel, the truncus arteriosus must be divided. A septum forms across the truncus from two lateral ridges. At the distal end of the truncus, furthest from the heart, the plane in which they lie is at right angles to the antero-posterior plane of the body. The ridges run towards the heart down the inside of the bulbus in a spiral manner; that on the right passing behind, and that on the left passing in front, giving the septum formed by their fusion a twist in a clockwise direction through 270°, nearly a complete rotation. Thus it comes about that the *posterior* division of the tube comes ultimately to lie on the *right* hand side; and the *anterior* division on the *left* (Fig. 3.) This rotation, although ultimately modified, gives rise to the normal position of the aorta and pulmonary artery: the pulmonary artery arises in front from the right ventricle and passes to the left and behind. The two circulations are now "crossed" as well as "in parallel."



FIG 3
Torsion of bulbar septum
(After J. W Brown)

The septum of the truncus, called the aortico-pulmonary septum, becomes continuous with that end of the bulbar septum, which is distal or furthest from the heart, at the point where the semilunar valves appear. The distal part of the bulbar septum fuses, nearer the heart, with the proximal part of the bulbar septum, and this joins with the interventricular septum. Th[illegible]

their [illegible]

The bu[illegible]

The critical period of development lies within the fifth and eighth weeks. During this time the septa of the auricles and ventricles are forming, and the rotation of the septum in the truncus and bulbus takes place; the cardiac septum fuses with the bulbar; and the bulbus cordis disappears. Many defects arise from the imperfect completion of these changes, and for this reason the defects are finally often multiple.

Defective rotation of the bulbus and truncus will result in a *faulty position (transposition) of the aorta and pulmonary artery*. The septum may not develop and a primitive single truncus persist. Dextroposition of the aorta may result from transposition; or perhaps from the persistence of the primitive right aorta (there are two aortas in crocodiles), the left having disappeared or fused with it (5).

The Absorption of the Bulbus Cordis. The bulbus persists in fishes as a separate chamber between the ventricle and the aorta In the human heart the part embedded in the bulbo-ventricular groove, which forms the bulbo-ventricular ridge, ultimately disappears. A certain amount of untwisting or detorsion of the tube occurs at this spot, which is called the bulbo-ventricular loop. This is an important change and is connected with the absorption of the bulbus (7). If the embedding of the bulbus in its groove is faulty, the twisting will be imperfect and transposition results (8). Most of the bulbus is absorbed into the right ventricle to form ultimately its conus arteriosus or infundibulum If this process is imperfect, stenosis and hypoplasia of the infundibular part of the conus and of the pulmonary artery result (4); in the tetrad this is associated with some degree of transposition or dextroposition of the aorta. A small part of the bulbus is absorbed into the left ventricle just below the aortic valves. Incomplete absorption here causes subaortic stenosis.

The Atrial Canal. Between the primitive auricle and ventricle lies the atrial canal. This is divided into two channels by the fusion of two endocardial swellings, which lie, one in front and one behind, to form a partition. The musculature of the auricles and ventricles, hitherto continuous, is divided by connective tissue growing in, so that only a few strands are left, which later become the bundle of His. This may be interrupted in congenital heart block. The septa of the auricles and ventricles fuse with these

endocardial swellings. *If they fail to develop defects in the septa* and auriculo-ventricular valves result.

The Interauricular Septum. In the fourth week the septum primum grows down from the upper and posterior part of the single primitive auricle towards the atrial canal. Here the edge of the concave lower margin fuses with the anterior and posterior endocardial swellings of the canal. But the central part of the septum, being concave, leaves an opening, the foramen primum. During the fifth week the upper part of the septum primum disappears and leaves a hole, the foramen secundum. *A second septum (secundum)* now appears to the right of the first septum and grows downwards, overlapping the first septum, closing the foramen primum and leaving a space opposite to *the foramen secundum*, which is the foramen ovale (Fig. 4). This allows blood to pass through from the right auricle to the left in the fœtal *circulation, and closes after birth. If it* remains widely open, one of the forms of interauricular or atrial septal defect results.

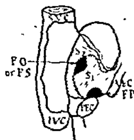


Fig. 4.

Formation of Interauricular Septum

S.V.C.	Superior vena cava
I V C	Inferior vena cava
F P	Foramen primum.
F O F S	Foramen ovale or secundum
S_1	Septum primum
S_2	Septum secundum
A E C.	*Anterior endo-cardialcushion.*
P.E C	Posterior endo-cardial cushion

(After Walmsley)

The Interventricular Septum. This develops in the fifth week as a ridge (septum inferus) in the floor of the primitive ventricle. Two cavities are hollowed *out on either side to form the ventricles,* right and left. The posterior part of the septum fuses with the posterior endo-*cardial* cushion in the atrial canal. The final fusion of *the upper part of the* interventricular septum with the proximal part of the septum dividing the bulbus cordis thus completes the partition of the right and left sides of the heart.

REFERENCES

1 ABBOTT (1936) *Atlas of Congenital Cardiac Disease.* New York.
2 DRY (1937) *Amer Heart J*, 14, 135
3 BROWN, J. W (1939). *Congenital Heart Disease*

the left ventricle was also much enlarged so that there was left axis deviation as though the pulmonary lesion had always caused a shunt from right to left (3).

Clinical Features. There may be nothing to draw attention to the lesion until well into adult life. When the effects are well developed there are signs of great enlargement of the right ventricle, extending far to the left (1). The enlarged pulmonary artery produces pulsation and diastolic shock, with loud second sound; often there is a systolic murmur and perhaps a diastolic murmur. It is doubtful whether the lesion itself can produce any sign at all.

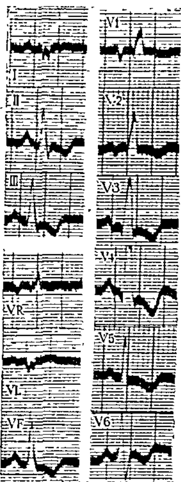


FIG 5

Right ventricular hypertrophy from a case of Lutembacher's Disease. Note delayed R-wave without S in V_1, V_2, V_3, V_4 and V_4. T-waves are negative in all chest leads. The heart is vertical

The radiological appearances confirm the large right ventricle and bulging left pulmonary artery, with the large branches of the right division visible to the right. The left branch of the pulmonary artery is seen from the front and in the left oblique position (5). Enlargement of the right auricle is stressed (4) but may not be always conspicuous, perhaps because it is rotated forwards (1).

Pulsation in the pulmonary artery, the "hilar dance," and in its branches is usually clearly seen, but is not pathognomonic for it is seen in pulmonary reflux and pulmonary arteriolitis and patent ductus arteriosus. The lung fields are not usually congested. The most notable and constant finding is the great enlargement of the pulmonary artery and its branches (Plate 1).

The aorta appears to be small. The cardiogram shows the hypertrophy of the right venticle (Fig. 5).

To face p. 8.







A
Atrial Septal Defect; early phase.

PLATE 1

B
Atrial Septal Defect; late phase.

Atrial septal defect is the only congenital lesion in which auricular fibrillation is at all common. Flutter is also met with (5) Paralysis of the left recurrent laryngeal nerve from pressure of the large pulmonary artery has occurred (6).

ATRIAL SEPTAL DEFECT AND MITRAL STENOSIS. (Lutembacher, 1916.) (M. Abbott, 1915.) Almost all the cases occur in women (7) The signs are those of mitral stenosis and atrial septal defect. One accentuates the other. There will be more tendency to enlargement of the right auricle and engorgement of the lungs. In one sense the defect relieves the left auricle in the face of mitral stenosis, for it may not be enlarged. In the other it further overloads the right ventricle Perhaps it is beneficial. It has been suggested that modern surgery might provide a relief for gross mitral stenosis in this way (2). A further suggestion is that as the left auricle lies above the right, the effect of gravity, apart from pressure, decides the filling of the right auricle, whether mitral stenosis is present or not (8). Mitral stenosis does not seem to alter the course of the disease, but may increase the tendency to fibrillation (9).

COURSE AND PROGNOSIS. In atrial septal defect the onset of dyspnoea may be delayed well into adult life. Gradually failure of the right heart comes on, frequently with the development of fibrillation. Probably half of them pass the age of 40 (10). Many patients have reached advanced years. Bacterial infection is very uncommon.

REFERENCES

1 BEDFORD, PAPP, PARKINSON (1941) *Brit Heart J*, 3, 37
2 O'FARRELL (1941) *Irish J. Med Sci*, 6, 597
3 WOOD, P (1942) *Brit Heart J*, 4, 11
4 COSSIO, ARANA (1937). *Bull Acad Med Paris*, 117, 212
5 LAUBRY *et al* (1939). *Radiologie Clinique du Coeur et des gros Vaisseaux.* Paris
6 ROSLER (1934) *Arch int Med*, 54, 339
7 MCGINN, WHITE (1933) *Amer Heart J*, 9, 1
8 UHLEG (1942) *Amer. Heart J*, 24, 315
9 BARRETT, J B, WHITE, P. D (1945) *Amer. J. Med Sci*, 209, 355
10 ERLANGER, H, LEVINE, S A (1943) *Amer Heart J*, 26, 520

Isolated Ventricular Septal Defect

(*Maladie de Roger*)

As an isolated lesion this is one of the commonest congenital

Embryology. The ventricular septum is formed in its upper and anterior part from the septum which divides the proximal end of the bulbus cordis. The rest is derived in its lower part from the septum inferius of the ventricle and the cushion of the atrial canal in its upper and posterior part. The membranous part marks the junction of these two elements. The commonest place for an opening is just in front of the membranous part. Elsewhere it is rare to find defects: a hole near the apex recalls the heart of the python. It is not known why the septum fails to form completely.

The hole may be anything up to a centimetre across, and the margin is usually fibrous, unlike that of the opening in the tetralogy which is fleshy (2). It is evident that the isolated ventricular septal defect is different in character from the hole in that condition, where failure in the rotation of the septum of the bulbus cordis is the cause. The fibrosis may involve the adjacent aortic cusp and cause aortic incompetence (3). The bundle of His may be involved and complete heart block results. A left to right shunt will occur. The intra-cardiac catheter shows that arterial blood is present in the right ventricle (6, 7), unless the pressure rises on the right side sufficiently high to reverse it, then only will cyanosis appear. *Thickening of the endocardium of the right* ventricle is seen where the jet of blood impinges opposite to the hole

Clinical Features. The typical signs are a harsh systolic murmur, and a strong thrill, loudest in the fourth space just to the left of the sternum. Usually there is no cardiac enlargement, or change in the cardiac outline at first. Occasionally the heart becomes rather globular in form and the pulmonary artery enlarges The cardiogram shows no constant abnormality. There is usually little or no physical disability, and an ordinary life can be enjoyed It is possible that the hole may close in the first two years of life (4, 5). We have seen such a case. The chief danger is bacterial infection at the site of the lesion. Patients usually reach the forties, or over. (Plate 2.)

REFERENCES

1 Muir, Brown (1934) *Arch Dis Child*, 9, 27
2. Brown (1939) *Congenital Heart Disease*, London
3. [illegible] *[illegible] de Médecine*, 50, 439
4. [illegible]
5 [illegible] ed, 30, 698
6. [illegible] 152
7. [illegible] d *Assoc. J*. 56, 249.

Aneurysm of the Interventricular Septum

See under Transposition of Aorta.

Congenital Heart Block. This abnormality finds a place here, as many cases are met with in isolated ventricular septal defect. About the fifth week of fœtal life the anterior and posterior endocardial cushions fuse to form the atrio-ventricular canal. As the atrial ring develops the muscle of the auricle and ventricle is separated except for the fibres which become the bundle of His The bundle may be interrupted by fibrous tissue in this process (1). Actually, the septum is completed at the eighth week, and the hole, if present, will be anterior to the membranous part; hence most cases of patent septum are seen without heart block. But it has been noted that when the membranous part is affected there may be block, for the bundle lies near (2). Probably the important point is involvement of the upper part of the bundle or node in excessive fibrosis (3). Atrial septal defect may be present as well (4). Clinically, these cases may easily escape diagnosis for the ventricular rate is often over 50. The lesion has been diagnosed in utero by means of sound records (9) The blood pressure may be rather high (5). There may be a fair acceleration on exercise. Atropine may cause a considerable increase in rate (6). Adrenalin may not accelerate the heart rate, but it may rise with fever. In this case there was congenital dextrocardia (7). Stokes-Adams attacks are rare, but syncopal attacks in childhood should arouse suspicions of the condition. The patients are perhaps likely to die suddenly, although they have very fair capacity for exertion. Not many cases have been recorded over the age of twenty, but by that time the congenital nature is hard to prove. A series of seven cases, however, have been followed for a number of years and none have showed any disability. The prognosis appears to be very good if no other lesions are present. (8).

REFERENCES

1 Yates, Libman, Cornell (1934). *J. Amer Med Assoc.*, 102, 1660
2 Yates, Lyon, McNabb (1933) *J Amer. Med Assoc*, 100, 1831.
3 Stein, Uhr (1942) *Brit. Heart J*
4 Peel (1945). *Brit Heart J.*, 5, 11.
5 Campbell, Suzman (1934) *Amer Heart J.*, 9, 304
6 Bower (1939) *Lancet* 2, 686
7 Leys (1943) *Brit. Heart J*, 5, 8
8 Campbell (1943) *Brit Heart J*, 5, 15
9 Jordan, Randolph (1947) *Amer. Heart J.*, 33, 109

Defects of Aortic Septum

In normal development the truncus arteriosus is divided by its spiral septum into the aorta and pulmonary artery. Sometimes this division is incomplete. Brown (1) classifies these into three groups :—

1. Persistent truncus arteriosus, where there is no septum at all.
2. Partial deficiency of septum, so that aorta and pulmonary artery communicate.
3. Aneurysm of a sinus of Valsalva.

1. **Persistent Truncus Arteriosus.** The defective development of the aortico-pulmonary septum is always associated with some degree of abnormal torsion (2). As the cusps of the aortic and pulmonary orifices are normally developed from four buds, the presence of four valve cusps is the definite sign that the single trunk is the true primitive truncus arteriosus. There should be no remnants of any other trunk and the vessel must supply the lungs and systemic circulation. But three cusps are sometimes seen, as in a case where the pulmonary artery branched off the common trunk. This is type 4 of Humphreys (10). A similar case had the blood supply to the lungs from a branch arising from the ductus arteriosus (12).

In a typical case the large vessel will arise, sometimes rather to the right, above a ventricle whose septum is incomplete. The heart will be enlarged, the cardiogram usually showing right axis deviation. No typical murmurs are mentioned (3). There will be more or less cyanosis. This depends on the relationship of the vessel to the septum. The aorta may run to the right, or divide to form a double aortic arch (4). Survival to adult life is possible; infection may occur.

This must be contrasted with the findings in a case of a common aorto-pulmonary trunk. Here the patient, aged 18, was cyanosed. The aortic and pulmonary valves were normal. The skiagram showed a remarkably enlarged aorto-pulmonary sac (11).

2. A partial deficiency of the aorto-pulmonary septum is due, when just at the level of the valves, to failure of this septum to unite with the bulbar septum. Blood will then pass with continuous murmur into the pulmonary artery, causing its enlargement. Cyanosis may develop late. Infection may occur.

The defect in the septum may be present as an aneurysmal thinning, and rupture in after life, causing an intense roaring, persistent murmur and failure of the right ventricle (5).

3. Aneurysms usually affect the right or anterior sinus. Aneurysm of the right sinus of Valsalva may rupture into the right ventricle. These aneurysms may be multiple and affect all three sinuses, and cause heart block by pressure on the bundle of His (6). They may rupture fatally. In one interesting case an aneurysm from an anterior sinus ruptured into the right auricle and caused congestive failure (7). Rupture of an aneurysm of the posterior sinus has been recorded with the same effect (8). Another in a similar situation, perhaps with acquired degenerative changes, caused complete heart block. (9) These aneurysms may be seen in the skiagram, and one arising from the left sinus must be differentiated from aneurysm of the left ventricle.

REFERENCES

1 BROWN, J. W (1939) *Congenital Heart Disease* London
2
3 *ngenital Heart Disease.*
4
5
6
7
8
9
10 ... (1943) *Brit Heart J*, 5 191
11 BAIN, PARKINSON (1943) *Brit Heart J*, 5, 97.
12 PRATT-THOMAS (1947) *Amer Heart J*, 34, 292.

Transposition of the Great Vessels

This was found sixty-nine times in the thousand cases listed in Abbott's Atlas.

In complete transposition, the aorta lies in front of the pulmonary artery and arises from the right ventricle; the pulmonary artery lies behind, arising from the left ventricle. This is an extreme example of the abnormality. Rokitansky in 1875 first supposed that these cases of transposition were due to anomalous rotation of the septum which divides the truncus arteriosus. Normally, this septum runs a spiral course, finally through 150° in a clockwise sense. This is evident when one considers how the pulmonary artery and aorta are wrapped round each other in the normal heart; so that the pulmonary artery comes from the

left, forwards to the right, into the right ventricle. Keith (1909) stressed the importance of the complete absorption of part of the bulbus cordis into the right ventricle; *faulty absorption tends to* pulmonary stenosis, and this defect is often associated with some degree of transposition. Spitzer (1923) suggested that when torsion was incomplete, the left aorta disappeared and the primitive reptilian aorta was re-opened on the right side, causing dextro-position. *When torsion was less defective* both trunks might persist and fuse to form one central aorta. He distinguished these pathological types :—

Group 1. Riding aorta.

Group 2. Partial transposition—both vessels from right ventricle.

Group 3. No torsion. Complete transposition.

Group 4. Transposition with gross septal defect.

Lately more attention has been given to the part played by defective absorption of the bulbus, which interferes with torsion (1). The fault is located in the bulbo-auricular spur, the spot where the bulbus becomes embedded (2).

Some writers distinguish two phases in normal development :—

1. In the first the bulbus becomes looped and kinked, a twist occurs in it, causing the spiral septum which divides it longitudinally to run through 270°.
2. This phase marks the absorption of the bulbus cordis. At its distal orifice there is clockwise torsion of 150°, with some degree of backwards or anti-clockwise torsion of 45° at the proximal orifice, 105° in all, so the twist is reduced. The bulbus then becomes shorter or absorbed, and the arterial trunks are twisted finally about 150° round each other. If the process of absorption interferes with the degree of torsion, i.e., produces less twisting at the distal orifice and more back torsion at the proximal, the ultimate relative positions of pulmonary artery and aorta are abnormal and some degree of transposition results.

How far Spitzer's theory is correct in explaining defects, is not yet certain. One interesting series of cases with over-riding aorta have been analysed in favour of this view (3). Two others are described (4) which suggest a reopening of the primitive right aorta as the cause of the transposition.

Complete Transposition. If this happens and there is no patency of the cardiac septa or ductus, the left ventricle pumps blood to the lungs and the right to the body. Cyanosis is severe; life cannot be maintained (5). As there must be associated lesions for survival, Taussig (6) considered the clinical picture shows (1) the features of transposition (2) those of the other lesions, such as patent ductus, atrial septal defect, patent interventricular septum. There is persistent cyanosis, usually severe. This may not be gross if the blood does not mix. The right ventricle is enlarged. There is a peculiar shadow of the great vessels, seen on screening. As the aorta lies further to the right and in front, and the pulmonary artery further to the left and behind, the shadow is narrower in the antero-posterior view and wider in the left anterior oblique view; the reverse of the normal. This appearance may provide a diagnosis. A systolic murmur may be heard, or none at all if the septal hole is large. *Bicuspid* pulmonary valves are not uncommon and suggest the *reptilian state*. Auriculo-ventricular dissociation may occur (3).

In Arrested Transposition the aorta lies on the right, but arises from the correct ventricle, and the pulmonary artery lies to the left, arising from the right ventricle. The key to the correct diagnosis of the ventricle is the number of cusps in the auriculo-ventricular valve; but the arrangement of the Purkinje system also differs in each ventricle. Cyanosis may not be severe. These have a better outlook. Cases of transposition rarely live long. They are subject to bacterial infections.

Aneurysm of Interventricular Septum. A small sac projects under the tricuspid valve involving the membranous part of the septum. It is probably associated with defective development of the upper part of the septum due to slight dextraposition of the aorta.

REFERENCES

Keith (1909) *Lancet*, 2, 359

5 Ingham, Willins (1939) *Amer. Heart J.*, 15, 482
6 Taussig (1938) *Amer. Heart J.*, 16, 728

Pulmonary Stenosis and Atresia

Stenosis at the pulmonary orifice is due to more than one cause and may be associated with other lesions in a most interesting way.

1. There is a local fibrotic valvular lesion, of uncertain origin, which probably develops fairly late in fœtal life. It is associated with enlargement of the pulmonary artery, and not uncommonly the ductus arteriosus is patent. The obstruction may amount to atresia.
2. The whole conus may be hypoplastic, with stenosis at its lower end—infundibular stenosis. This abnormality arises early in fœtal life, about the fifth week, when the bulbus *cordis is undergoing absorption.*
3. At this time torsion of the bulbus is taking place and its spiral septum is forming, as well as the ventricular septum, and these ultimately fuse by the sixth week. It is not surprising, therefore, that a combination of defects can arise, such as transposition of the great vessels, particularly dextroposition of the aorta, patent ventricular septum and pulmonary stenosis of the conus type; or dextroposition of the aorta and septal patency may appear alone (Eisenmenger).

As cyanosis develops sooner or later *in all* these cases, they have been classed as cyanotic, or late cyanotic.

Pulmonary Stenosis WITH PATENT VENTRICULAR SEPTUM. This is the commonest congenital defect in which cyanosis is conspicuous, and yet the patients reach adult life and may live many years. First described by an English physician, Peacock, in 1866, the combination of four associated abnormalities has become associated with the name of Fallot (1888). The tetrad consists of:—

1. Hypoplasia, stenosis, or atresia of the pulmonary artery.
2. Interventricular septal defect.
3. Dextroposition of the aorta.
4. Hypertrophy of the right ventricle.

1. The pulmonary conus may be the site of infundibular stenosis; or the whole conus and artery may be hypoplastic. The valves may be well formed and are often bicuspid, as in reptiles.

PLATE 3

[illegible]

To face p. 16

Pulmonary Stenosis and Atresia

Stenosis at the pulmonary orifice is *due to more than one cause* and may be associated with other lesions in a most interesting way.

1. *There is a local fibrotic valvular lesion*, *of uncertain origin*, which probably develops fairly late in fœtal life. It is associated with enlargement of the pulmonary artery, and *not uncommonly the ductus arteriosus is patent.* The obstruction may amount to atresia.
2. The whole conus may be hypoplastic, with stenosis at its lower end—infundibular stenosis. This abnormality arises early in fœtal life, about the fifth week, when the bulbus cordis is undergoing absorption.
3. At this time torsion of the bulbus is taking place and its spiral septum is forming, as well as the ventricular septum, and these ultimately fuse by the sixth week. It is not surprising, therefore, that a combination of defects can arise, such as transposition of the great vessels, particularly dextroposition of the aorta, patent ventricular septum and pulmonary stenosis of the conus type; or dextroposition of the aorta and septal patency may appear alone (Eisenmenger).

As cyanosis develops sooner or later in all these cases, they have been classed as cyanotic, or late cyanotic.

Pulmonary Stenosis WITH PATENT VENTRICULAR SEPTUM. This is the commonest congenital defect in which cyanosis is conspicuous, and yet the patients reach adult life and may live many years. First described by an English physician, Peacock, in 1866, the combination of four associated abnormalities has become associated with the name of Fallot (1888). The tetrad consists of:—

1. Hypoplasia, stenosis, or atresia of the pulmonary artery.
2. Interventricular septal defect.
3. Dextroposition of the aorta.
4. Hypertrophy of the right ventricle.

1. The pulmonary conus may be the site of infundibular stenosis; or the whole conus and artery may be hypoplastic. The valves may be well formed and are often bicuspid, as in reptiles.

all cases (9)—otherwise they cannot be differentiated. As a consequence of the lesion there is evidence of more or less hypertrophy of the right ventricle clinically, and in the electrocardiogram. Cyanosis is absent as a rule for some years, or only slight; but will usually become progressive as the right ventricle fails. They thus come into the class of late cyanosis. A patent ductus may also be found, or a patent auricular septum (9).

Bacterial infection is common in either type, and so is phthisis (10). The average age of death is given by Abbott as twenty-five years (11) though for long the lesion may be well borne, and we have seen several pass easily through pregnancy. Probably the average life is from thirty to forty years (12).

Pulmonary Atresia. Atresia of the pulmonary orifice may result from hypoplasia affecting the infundibulum and pulmonary artery, as in the tetralogy, or there may be complete closure of the valvular opening and hypoplasia of the artery above. In the latter the sixth arch has disappeared and the ductus is *closed*; in the former it may be open and supply blood to the lungs. Some cases are on record of adults where the blood reached the lungs only through huge bronchial arteries (13). These patients are very blue and have much clubbing. No murmur may be heard; the skiagram shows a concavity in place of the pulmonary bulge. The clinical diagnosis is possible on these findings. The absence of murmur and thrill is against the diagnosis of the tetrad, although the skiagram suggests it. A similar adult case, with slight murmur, died of cerebral thrombosis (13).

When there is pulmonary atresia and a closed ventricular septum the circulation may be maintained by a patent auricular septum and a patent ductus arteriosus. The condition is against long survival.

Eisenmenger Complex (1897). This rare combination of defects is embryologically related to the others in this group. There is the same dextroposition of a sometimes small aorta, which may be truly a right-sided arch (14) with a large hole in the ventricular septum. One may infer that the original defect lay in the torsion of the bulbar septum and its failure in consequence to unite with the ventricular septum (15). There is, however, no hypoplasia or stenosis of the conus arteriosus or pulmonary artery, which is in fact large. Pulsation of the pulmonary artery is conspicuous, its cusps may even be incompetent (16). The right

faint. These cases develop bacterial infections; emboli may be discharged into both circulations (5). The valves of the dilated aorta may become incompetent. Clubbing of the fingers, even to osteoarthropathy, usually parallels the cyanosis and polycythæmia (19).

Generally speaking the patients are poorly developed and are much limited in their capacity for exertion. They often stay crouching on the floor. Cerebral disturbances like epilepsy are not uncommon. Tuberculosis is frequent. Cases of hemiplegia in infants have been reported (6)—perhaps thrombotic or embolic. Many live for a surprisingly long time, well past middle age.

Pulmonary Stenosis WITH THE INTERVENTRICULAR SEPTUM CLOSED.

Valvular Type. These cases are not very uncommon. There is a ring of fibrosis at the level of the valves. As a result there is a diaphragm or cone, with a small opening in the middle. Fibrosis may extend into the muscle of the conus adjacent. This fibrosis has been said to be the result of fœtal endocarditis—an unsatisfactory explanation, for we are unaware of any evidence showing an acute phase. Gross (7) considers that these lesions are not inflammatory, as true residues of this nature are not detectable. The absence of a patent septum between the ventricles suggests that the defect develops after the eighth week of fœtal life.

Conus or Infundibular Type. Keith has explained this lesion as a failure for the bulbus to become absorbed in the right ventricle. A small chamber occupies the place of the conus arteriosus, communicating below with an enlarged right ventricle, and with a dilated pulmonary artery above, guarded by more or less normal valves (8). The lining of the infundibulum is usually thickened. In some cases the ventricular septum is patent. The aorta is somewhat dextroposed.

In both these types the pulmonary artery, for some unknown reason, is often conspicuously enlarged and its walls are thin, and it shows very prominently in the skiagram (Plate 1).

Physical signs are a local systolic murmur conducted up and to the left, and a thrill, rather lower down in the infundibular type, and probably some systolic pulsation and dulness over the pulmonary artery. Probably the second pulmonary sound is audible in the conus type—some find the second sound loud in



PLATE 5

Eisenmenger Complex.

To face p 20

ventricle is enlarged, so that the electrocardiogram usually shows right axis deviation. A systolic murmur and thrill are usually present. Cyanosis is usually severe, depending on the shunt, but may not be so. Physical disability may not be severe; so that survival may be fairly long (17). Bacterial infection may occur. (Plate 5.)

SURGICAL TREATMENT. When restriction of the flow of blood to the lungs is the important defect, it has been found possible to remedy this to some extent by implanting the right subclavian artery into the main pulmonary artery. The circulation to the arm is not at all impaired. There is decided improvement in the patient. Pulmonary stenosis of the Fallot type and atresia should be selected. It is important to be sure the pressure in the pulmonary artery is low, as it should be in these cases—and so exclude other cyanotic cases For this an estimation with a manometer was made, using a needle in the artery. The mortality is 16 per cent, but is now decreasing (18).

It is possible, by implanting an artery, to raise the oxygen saturation from between 30 and 40 per cent to between 65 and 75 per cent. The hæmoglobin and red cell count falls to normal, the clubbing disappears, and the child becomes normally active (20). It must be remembered that the heart is still very much deformed, even if cyanosis is reduced A still further abnormality is added, comparable to the patent ductus arteriosus and no doubt it is liable to infection, a lesion which surgeons are at pains to remedy in other cases.

REFERENCES

1 PRINZMETAL (1941) *J clin Invest*, 20, 705
2 TALBOT *et al* (1941) *Amer Heart J*, 22, 754
3 MCGUIRE, GOLDMAN (1937). *Amer Heart J*, 14, 230
4 FLEURY (1937) *Arch Mal Cœur* 30, 121
5 HERNDON VASS, DONOVAN (1939) *Amer Heart J*, 17, 553
6 CORNER, PERRY (1942) *Brit Heart J*, 4, 121
7 GROSS, P (1941) *Arch Path*, 31, 163
8 DRYFRRE, WALMSLEY (1939) *Brit Heart J*, 1, 325
9 CURRENS (1945) *Amer Heart J*, 30, 491
10 AUERBACK, STEMMERMANN (1944) *Amer J med Sci*, 207, 219
11. ABBOTT (1936) *Atlas of Congenital Heart Disease*
12. HUNTER, LIPSCOMB (1942) *Brit Heart J*, 4, 124
13. EAST, BARNARD (1938) *Lancet*, 1, 834
14 GLAZEBROOK (1943) *Brit Heart J*, 5, 147
15 ROSEDALE (1935) *Amer J Path*, 11, 33
16 TALLEY, FOWLER (1936) *Amer J med Sci*, 191, 618
17 STEWART, CRAWFORD (1933) *Amer J Path*, 9, 637
18 BLALOCK, B H. (1946) *Bull New York Acad Med*, 22, 57
19 MEANS, BROWN (1947) *Amer Heart J.*, 34, 262
20 TAUSSIG, BLALOCK (1947). *Amer. Heart J*, 33, 413.



PLATE 5
Eisenmenger Complex.

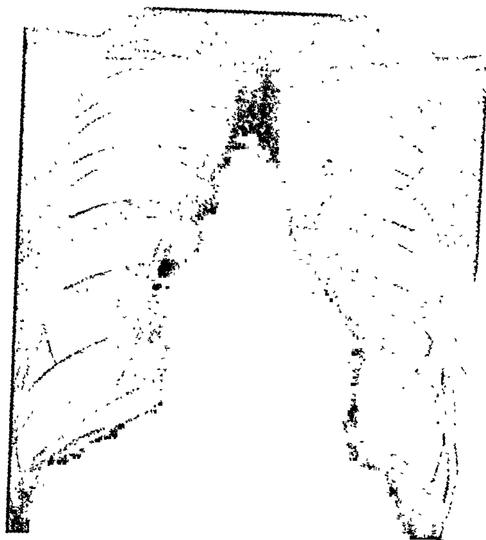


PLATE 6

Subaortic Stenosis.

Sub-aortic Stenosis. This lesion is due to imperfect involution of that portion of the bulbus cordis which takes part in the formation of the left ventricle just below the aortic valves. The defect is homologous to conus or infundibular stenosis in the right ventricle, into which most of the bulbus is absorbed. A fibrous ridge or bar is seen just below the semilunar valves which contains a good deal of elastic tissue. Occasionally there may be stenosis of the valves as well. Coarctation may be present in the aorta. The usual systolic murmur and thrill are produced: but the obstruction is not often severe enough to cause much left ventricular hypertrophy, so the cardiogram may not show left axis deviation. For the same reason the anacrotic type of pulse is not felt, and the blood pressure may not be low (1). The aortic second sound will be clearly audible (2). There may be but little physical disability. There is a distinct danger of bacterial infection at the site of the lesion. (Plate 6.)

REFERENCES

1 Brown, J. W. (1939) *Congenital Heart Disease* London
2 Young, D. (1944) *Amer Heart J*, 28, 440

Aortic Stenosis: Valvular Type. In this case the lesion is at the valves, and the defect is homologous to the valvular type of pulmonary stenosis. The aortic valves arise from the bulbar swellings, at the proximal part of the bulbus in the seventh week. Finally the valves appear to be fused and thickened. This state may result from faulty development, or possibly from "fœtal endocarditis." Aortic incompetence may also result from this defect.

As the obstruction may be severe, all the local signs of stenosis will be correspondingly conspicuous, and the anacrotic pulse will be felt. The aortic second sound will be faint or inaudible: the left ventricle will show appropriate hypertrophy, which is likely to cause left axis deviation in the cardiogram. There may be some dilatation of the aorta just above the valves, as there is in the homologous pulmonary stenosis above the valves. There may be poor physique, but the lesion is often well borne. Danger of bacterial infection is considerable.

Abnormal Semilunar Valves. The aortic and pulmonary valves are developed from four endocardial cushions which are present at the spot where the bulbus cordis joins the truncus

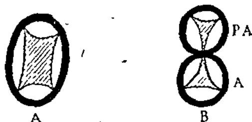


Fig 6
Formation of the semi-lunar valves
(After J W Brown)

arteriosus. The distal bulbar septum divides the tube into two, and also divides the four cushions into six. There are then three in each tube (Fig. 6). If the division of the cushion is faulty, two may persist only in the aorta, giving a bicuspid aortic valve (Fig. 7). or a supernumerary cushion, or two, may produce

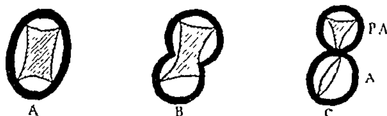


Fig 7
Formation of biscupid aortic valves
(After J W Brown)

extra pulmonary cusps (*Fig. 8*). Spitzer's explanation for the bicuspid aortic valve in the tetrad, where there is transposition, is that it represents the primitive reptilian right aorta, which has two valves. Bicuspid aortic valves are closely associated with abnormalities of the aortic arch, such as coarctation, patent ductus, sub-aortic stenosis, and aortic and ventricular septal defects.



Fig 8
Formation of supernumerary cusps in pulmonary artery
(After J W Brown)

Bicuspid pulmonary valves occur in infundibular stenosis and in the tetrad. They are not liable to infection or to calcification (1). Even when there are four or five pulmonary cusps they may function quite well, but three are probably the most efficient. A supernumerary cusp, or cusps, might be suspected when there is unexplained pulmonary incompetence (3) (Fig. 8).

The defect in bicuspid aortic valves was shown to be associated with an abnormal position of the elastic tissue in relation to the annulus fibrosus where it lay superficially at the raphe which represents the abortive commissure. Osler, many years ago, pointed out that the low raphe was characteristic, and that the sinuses were equal. The presence of a ridge on the wall of the aorta at the commissure, slightly involving the sinus and composed of elastic tissue, is said to be characteristic of the congenital defect (4).

It may be difficult to distinguish the acquired from the congenital types It is suggested that rheumatic infection may be responsible for those cases where no other congenital defect is present According to Gross (5), the commissural lesion in acute rheumatism may cause fusion of the adjacent cusps (6), and the subjacent scarring may mimic the condition described by Lewis and Grant. The raphe in the bicuspid valve contains collagenous tissue and not elastic, and there are other signs of past inflammation. These are the lesions peculiarly liable to infection and calcification (6).

Probably both types in time tend to become calcified and infected. Distinction can only be made by histological examination and this may not be easy owing to gross changes due to the calcification. The senile fibro-calcareous aortic stenosis, often seen in old men, may be the final result of these lesions in many cases

REFERENCES

1 Koletsky (1941) *Arch Path*, 31, 338
2 Lewis, T., Grant (1923) *Heart*, 10, 31.
3 Kissin (1936) *Amer. Heart J.*, 12, 206
4. Koletsky (1941) *Arch int Med*, 67, 129
5 Gross, L (1937). *Arch Path*, 23, 350
6 Gross, Silverman (1937) *Amer. J. Path*, 13, 350.

Abnormalities of the Aortic Arch

In the normal course of development the fourth arch on the left side persists to form the arch of the aorta, and on the right side it is represented in part by the innominate artery and some of the right subclavian.

Possibly through stenosis or some other cause, the left arch may disappear, wholly or in part, and the right arch persist instead, as it does in birds. Perhaps this stenosis leads to coarctation if it occurs after the right arch has disappeared (1). Occasionally, both arches persist complete.

Three types of abnormality may be distinguished (1):—

1. Right-sided aortic arch (avian).
2. Right-sided aortic arch with persistent left root.
3. Double aortic arch (reptilian).

The degree of persistence of the left arch distinguishes these three.

1. The aortic arch passes to the right of the trachea and œsophagus over the right bronchus, and then downwards, crossing behind the œsophagus still lower, to leave the thorax by the usual opening (Fig. 9A). Alternatively, the aorta may persist on the right side throughout its thoracic course.

The left subclavian artery (representing the left arch) may rise from the aortic arch and pass to the left in front of the trachea (Fig. 9B). The ductus arises from it, or from the aorta. Thus a vascular ring is formed round the trachea and œsophagus (2). The œsophagus is not pushed forward. The left subclavian artery may pass behind the œsophagus. The impression on the œsophagus filled with barium gives the diagnosis (7).

2. If the proximal part of the left arch persists, a diverticulum is formed at the end of the arch—persistent left root (1). The left subclavian arises from the diverticulum and runs behind the trachea and œsophagus. This vessel and the diverticulum push these structures forward.

The radiological findings are characteristic (2)

There is usually no aortic knob on the left: the aortic arch projects to the right as a knob or band. The persistent left root of the left arch may appear as a small knob on the left, thus two knobs may be seen. Barium in the œsophagus shows the relations

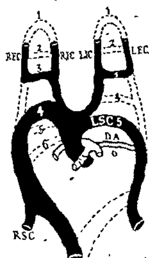


FIG 9A

Right aortic arch
R S C Right subclavian artery,
L S C Left subclavian artery
D A Ductus arteriosus
P A Pulmonary artery

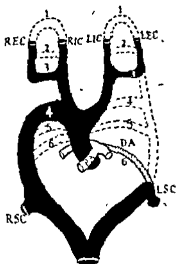


FIG 9B

Right aortic arch with persistent left root
L S C Left subclavian artery
D A Ductus arteriosus.
(After J W Brown)

very well (3). The ductus arises from the *diverticulum* and completes the vascular ring. The trachea is pushed to the left, and the right bronchus tends to point downwards instead of across—inversion of trachea (5).

3. There may be a double arch. The two arches meet behind the œsophagus to form the descending aorta. Each arch gives off its appropriate branches. The left is anterior and smaller.

The diagnosis is purely radiological.

Physical signs are suggestive but not definite. There may be dullness to the right of the sternum. The aortic second sound is heard high up. There may be some pulsation over the dull area. There may be a tracheal tug. These all suggest also aneurysm. Paralysis of the vocal chords may occur (2).

There is a curious association with the Eisenmenger complex (2) and with the tetrad of Fallot, a condition which was first recognised by Corvisart. The curve of the pulmonary artery may be prominent in the antero posterior view (6).

There are no symptoms as a rule except, rarely, dysphagia, called "lusoria," although it is genuine enough. In children stridor has been noticed. This is made worse by feeding. Barium in the œsophagus shows an impression on both sides (7).

A right subclavian artery may rise from the descending arch and pass behind the œsophagus. It does not affect this structure (3) nor cause symptoms (4).

REFERENCES

1 ARKIN (1936) *Amer Heart J*, 11, 444.
2 BEDFORD, PARKINSON (1936). *Brit J Radiol*, 108, 776
3 EVANS, W (1936) *Course of Oesophagus in Health and Disease M R C, Special Report Series*, No 208
4 DORGOPAL (1937) *J Tech Meth*, 17, 106
5 LIAN, MARCHAL (1937) *Arch Mal Cœur*, 30, 649
6 COSSIO, KREUTZER (1937). *Revista Argentina de Cardiologia*, 4, 177
7 NEUHAUSER (1946) *Amer J Röntgenol*, 56, 1

Coarctation of the Aorta

The earliest classification by Bonnet (1903) recognised two types, the infantile which was a diffuse narrowing of the aortic isthmus, and the adult which was a sudden constriction distal to the mouth of the left subclavian, near the origin of the ductus arteriosus. This is the important one. The constriction may amount to atresia, and may be associated with a patent ductus arteriosus. Three commoner types have been defined (1):—

1. Stenosis of arch, hypoplasia proximal to stenosis, ductus patent.
2. Stenosis of arch, hypertrophy proximal to stenosis, ductus closed.
3. Atresia of arch, hypertrophy proximal to stenosis, ductus closed.

These account for most of the adult cases.

Pathogenesis. The adult type of coarctation has never been found before or at birth. It has been supposed that the process of the closing of the ductus involves the wall of the aorta; and there is some histological evidence for this. (2) But sometimes the constriction is not so near, and also the ductus may remain open. It is significant that the defect arises at the junction of the fourth and sixth primitive arches. The matter is still obscure.

ANOMALOUS DEVELOPMENT OF THE AORTIC ARCHES. Of the primitive six pairs of aortic arches, the first three cephalic pairs

disappear. The fourth arch on the left side becomes the arch of the aorta; on the right side it forms the innominate, and part of the right subclavian arteries. The fifth arches disappear: the right sixth arch gives rise to the pulmonary artery, and the left to the ductus arteriosus (Fig. 10)

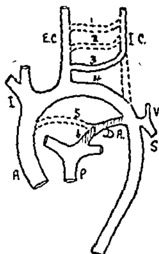


Fig 10

Development of left aortic arches Dotted lines indicate vestigial arches Numerals indicate the six arches
A Aorta
I Innominate
E C External carotid
I C Internal carotid
P. Pulmonary artery
D A Ductus arteriosus
V Vertebral artery
S Left subclavian artery
(After Evans)

Associated with these changes the following anomalies may occur:—

1. The right arch may persist instead of the left, causing a right-sided aorta.

2. Stenosis of the fourth left arch may lead to persistence of the right arch, or else to coarctation of the aorta.

3 Patent ductus arteriosus may be considered here, although its failure to close is more likely to be connected with events at or soon after birth. But its association with other lesions is so common that its patency may be due to earlier causes as well (Fig 11).

4. Double aortic arches may persist.

5 Anomalous branches of the aortic arch may be found.

At the site of coarctation the aorta may be completely closed as by a diaphragm, or there may be a small central hole of varying size. Sometimes the constriction is tapering, sometimes in the form of an hour glass (Fig. 12).

The radioscopy of the aorta in the left oblique position may reveal an absence of the arch (3) In the anterior view the posterior part of the arch (knob or knuckle) is flat as a rule (4), though sometimes it is prominent or double (28). The œsophagus may, when filled with barium, show two indentations, one above and one below the constriction. Pulsation of the aorta below the coarctation is reduced, as the kymograph shows (5). The constriction

There are no symptoms as a rule except, rarely, dysphagia, called "lusoria," although it is genuine enough. In children stridor has been noticed. This is made worse by feeding. Barium in the œsophagus shows an impression on both sides (7).

A right subclavian artery may rise from the descending arch and pass behind the œsophagus. It does not affect this structure (3) nor cause symptoms (4).

REFERENCES

1 ARKIN (1936) *Amer Heart J*, 11, 444
2 BEDFORD, PARKINSON (1936) *Brit J. Radiol*, 108, 776.
3 EVANS, W. (1936). *Course of Oesophagus in Health and Disease* M.R C.,
4
5
6 4, 177
7 NEUHAUSER (1946) *Amer. J Rontgenol*, 56, 1

Coarctation of the Aorta

The earliest classification by Bonnet (1903) recognised two types; the infantile which was a diffuse narrowing of the aortic isthmus, and the adult which was a sudden constriction distal to the mouth of the left subclavian, near the origin of the ductus arteriosus. This is the important one. The constriction may amount to atresia, and may be associated with a patent ductus arteriosus Three commoner types have been defined (1) :—

1. Stenosis of arch, hypoplasia proximal to stenosis, ductus patent.
2. Stenosis of arch, hypertrophy proximal to stenosis, ductus closed.
3. Atresia of arch, hypertrophy proximal to stenosis, ductus closed.

These account for most of the adult cases.

Pathogenesis. The adult type of coarctation has never been found before or at birth. It has been supposed that the process of the closing of the ductus involves the wall of the aorta ; and there is some histological evidence for this. (2) But sometimes the constriction is not so near, and also the ductus may remain open. It is significant that the defect arises at the junction of the fourth and sixth primitive arches. The matter is still obscure.

ANOMALOUS DEVELOPMENT OF THE AORTIC ARCHES. Of the primitive six pairs of aortic arches, the first three cephalic pairs

The High Blood Pressure. The cause of the high blood pressure proximal to the coarctation has aroused interest, and attracted attention to the kidneys. It is supposed that the obstruction is in some way responsible, and this may be associated with increased tone in the arterioles of the upper part of the body. It has been shown that there is actually a decrease in the renal blood flow, but a normal rate of glomerular filtration; in order to produce this it is suggested that there is spasm in the arteriole efferent from the glomerulus (13). A further suggestion is that the kidney is suffering from ischæmia of the Goldblatt type (14). Occlusion of the abdominal aorta in rats caused a rise in blood pressure (15). Direct measurement of the diastolic pressure in the legs has shown that it may be as high as that in the arms (14).

Symptoms associated with the high pressure are headache, giddiness, throbbing in the head, epistaxis. Aortic incompetence may result from the stretching of the aorta (4). The increased vascularity may lead to hyperthyroidism (29).

The cardiac output is increased in the majority of cases, but may be within normal limits unless failure has come on (16). The range of the figures for the peripheral blood flow was found to be increased on the average, indicating that a larger proportion of the cardiac output was allotted to the periphery (17).

THE COLLATERAL CIRCULATION. The obstruction leads to a lower systolic blood pressure in the legs than in the arms, and to weakening and retardation of the pulse in the legs: a delay of 0 03 second has been noted (3). Pulsation may be hardly palpable in the abdominal aorta and in the femorals. The collateral circulation has been well studied recently by Bramwell and Morgan Jones (18). The important features clinically are the tortuous pulsating arteries round the left shoulder, which are easily made out. They distinguish (1) scapular and cervical anastomoses, (2) internal mammary anastomoses, (3) intercostal anast[illegible]oses and (4) [illegible]

[illegible] demon-

to t[illegible]

bor[illegible] seen in the skiagram (19). The loops are conspicuous between fixed points in the arteries, at the angles of the ribs or further round, and are curiously symmetrical.

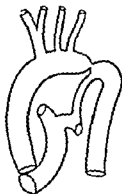

FIG 11
Coarctation of aorta
Patent ductus arteriosus


FIG 12.
Coarctation of aorta Ductus closed

of the aorta is well outlined by angeiocardiography, which also shows the delayed filling below it (27) (Plate 7).

CHANGES PROXIMAL to the OBSTRUCTION. There is a raised blood pressure in most cases (6). The proximal part of the aorta may be hypoplastic, but is more often dilated. Atheromatous degeneration in various stages is common, affecting also the branches. The aortic valves are often bicuspid (7) and may become calcified, and infected. They appear in some 40 per cent of cases (23). The blood pressure may be very different in the arms. This is due to anomalies in the great vessels; a weaker right pulse may be due to an abnormal origin of the right subclavian artery (8) or to stenosis at its origin (9). A weaker left pulse may be due to stenosis of the left subclavian (6); or to coarctation proximal to the origin of this vessel (10) which may cause enlargement of the right arm and shoulder (11). There is usually hypertrophy of the left ventricle, and this is apparent in the skiagram and in the electrocardiogram, which shows left axis deviation. These changes do not come in early years. Examination of the small arterioles of the skin and muscles of the arms showed no abnormalities; they were similar to those of the legs (12) But the subjects were young. Congenital defects in the cerebral arteries are common, giving rise to aneurysms, which may burst and cause subarachnoid hæmorrhage in one tenth of cases (23).

The upper part of the body tends to be well developed, with high complexion and warm moist hands.

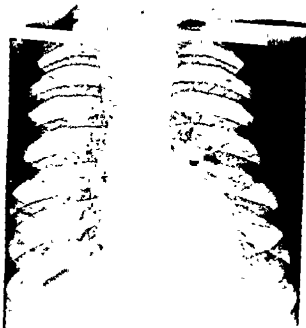


PLATE 7
Coarctation of Aorta.

To face p 30

It is supposed that pressure by the loops may cause thoracic pain in some cases. The notches do not appear in very young children as a rule.

The relatively poor blood supply to the legs and feet makes those parts cold and pale; patients complain of weakness of the legs on walking and intermittent claudication (20).

When the ductus arteriosus is patent, no collateral circulation develops (1). If the constriction is proximal to the left subclavian there are no anastomoses on the left side of the body. In the presence of a patent ductus the diagnosis is very difficult (28).

Clinical Features. The lesion was found 70 times in 1,000 cases (21). Males are more often affected than females. Symptoms often do not appear for years. Much depends on the degree of coarctation, the rise in blood pressure and the associated lesions, if any. Mild types, and they are perhaps commoner than supposed, may be missed clinically (22). A systolic murmur and thrill towards the base of the heart, and near the left clavicle or scapula, or an unexpected high blood pressure may draw attention to the lesion. Then all the other points are soon found. Heart failure may end a fifth of all cases (23), as a result of high pressure, perhaps aided by aortic reflux; but many escape it. The aorta may rupture in about this number; cerebral hæmorrhage from a congenital aneurysm may kill one third. Infection of the biscupid aortic valves (7) or of the area of coarctation is not uncommon. Thrombosis in an aneurysm at the site of a partly occluded ductus has been recorded (24).

Patients not uncommonly reach old age without trouble, if they pass the thirtieth year. Sudden strain is particularly dangerous (28). If symptoms occur early, death is likely to occur soon after the age of thirty (30).

Surgical Treatment. *The constriction had now been removed* and the cut ends of the aorta successfully anastomosed. Afterwards the blood pressure in the arms fell to normal. Pulsation returned to the arteries of the lower limbs. One patient died with sudden great dilatation of the heart, perhaps because the clamps were removed too quickly. These triumphs of vascular surgery offer great possibilities for the cure of this defect. Probably childhood will be the time to attempt them. Although many cases live long, the dangers are great (25, 26).

REFERENCES

1 Evans, W (1933) *Quart Jour Med*

, 903

, 14, 107

208

Inv Invest, 20, 107

145

18 Bramwell, Morgan Jones (1941) *Brit Heart J*, 3, 205

York

Patent Ductus Arteriosus

During fœtal life, before the use of the lungs necessitates a full pulmonary circulation, the blood passing into the pulmonary artery is carried into the aorta by the ductus arteriosus (Botalli). Closure of the ductus usually takes place soon after birth; after one month only 44 per cent are still patent, and after two months 12 per cent At the end of the eighth month 2 per cent of cases may still be open (1), but presumably may still close.

Ætiology. The method of closure is rather obscure; probably it is effected by a combination of causes (2) As the pulmonary circulation develops, the enlargement of the pulmonary artery and the expansion of the lungs may cause traction of the ductus. Kinking may occur at the same time, as it does in the new born lamb (3). The shunting through the lungs of much of the blood it carried lessens the force distending it. Possibly a neuro-muscular constricting influence is also at work. Finally, it is easy to see that an obliterative process is present by proliferation of its intima.



PLATE 8
Patent Ductus Arteriosus.

on the size of the arterio-venous shunt. A high pulse pressure at rest, increasing after exercise has been noted (8). The most important structural change is the enlargement of the pulmonary artery, easily seen on screening, and causing certain physical signs. (Plate 8.)

The effect on the individual varies. Some patients are well built, but some are described as weedy, pale, and of poor physique. Children are often backward and dull. There appears to be a definitely inhibiting effect on growth (29).

Cyanosis will not appear unless the shunt is reversed. This may occur transiently, on coughing or crying, or when the heart fails at the end. The lesion may therefore be classed with those causing "late cyanosis."

Clinical Diagnosis. The typical murmur (Gibson) is usually a continuous whizzing rushing sound, often rather hollow, loudest in the second left intercostal space near the edge of the sternum. It may be heard behind the back of the left shoulder. It is loudest just after the first heart sound, and usually continues through the second sound into diastole. Valsalva's experiment may diminish the diastolic phase. The diastolic part of the murmur is occasionally slight or absent in children The closure of the pulmonary valves is loud and often palpable. A thrill may be present in half the cases. The enlarged pulmonary artery may cause slight pulsation and an area of dullness near the sternum.

Radiological Findings. The important positive radiological findings are dilatation of the pulmonary artery. But this may be by no means conspicuous (9). The pulmonary arteries tend to be full and may pulsate freely. There may be increase in the pulsation of the ventricles, which may be enlarged; the left auricle may be dilated (10). It may be remarked that none of these *findings* may be conspicuous and helpful in the clinical diagnosis (Plate 7).

The electrocardiogram is usually normal; occasionally there is right axis deviation. The normal curve is important in confirming the diagnosis and excluding other lesions that may be associated.

The size of the ductus obviously cannot be gauged by the intensity of the murmur and thrill Probably the best indication is the size of the pulmonary artery and blood pressure readings (8).

Associated Lesions. Other congenital lesions have been found in two-thirds of all cases (11) We think that those who grow up

Why the ductus should fail to close is also obscure. It has been suggested that an abnormally obtuse angle of entry into the aorta may hinder closure (2); that it may have abnormally thin walls, which do not favour the obliterative process; that there is a defective neuro-muscular control. This last point is based on the large amount of muscle present in the middle coat. Atelectasis of the lung may play a part. The act of breathing is held to be an important factor in promoting closure, and oxygen must be in the air breathed (4). A hypoplasia of the aorta, or coarctation of the aorta, is not uncommonly found with patent ductus; so is pulmonary stenosis. This suggests some developmental anomaly reaching further back in fœtal life. There is some evidence to support a familial incidence (5). The lesion occurs much more often in female patients.

Effect on the Circulation and the Heart. The volume of blood passing into the pulmonary artery must depend on the bore of the ductus, which varies from one to five millimetres, or more—and perhaps upon the angle of its entry into the aorta. Cases of aneurysmal dilatation have been noted, presumably when the walls are very thin. Rarely, the ductus is so short that it amounts to little more than a direct anastomosis. As the pressure in the *aorta is higher than in the pulmonary artery, there will usually be* a persistent arterio-venous flow, most profuse soon after cardiac systole. It has been shown (6) that after experimental anastomosis the blood in the pulmonary artery has a higher oxygen content than before, and also higher than that in the right ventricle. From 45 per cent to 75 per cent of the blood leaving the left ventricle may pass through into the pulmonary artery. In order to maintain an adequate supply to the body the output of the left ventricle is increased and its work raised. Four times the amount of blood flowing through the right auricle went through the left auricle (7). The increase of pressure in the pulmonary artery will increase the work of the right ventricle. This pressure may be at thrice the normal level (27). There is, therefore, a tendency to increase the work of both ventricles, which will depend on the size of the ductus. Both ventricles may ultimately become enlarged. The blood pressure is not constantly affected: in any case it is very variable in children. Sometimes the systolic is raised and the diastolic lowered; possibly depending

on the size of the arterio-venous shunt. A high pulse pressure at rest, increasing after exercise has been noted (8). The most important structural change is the enlargement of the pulmonary artery, easily seen on screening, and causing certain physical signs (Plate 8).

The effect on the individual varies. Some patients are well built, but some are described as weedy, pale, and of poor physique. Children are often backward and dull. There appears to be a definitely inhibiting effect on growth (29).

Cyanosis will not appear unless the shunt is reversed. This may occur transiently, on coughing or crying, or when the heart fails at the end. The lesion may therefore be classed with those causing "late cyanosis."

Clinical Diagnosis. The typical murmur (Gibson) is usually a continuous whizzing rushing sound, often rather hollow, loudest in the second left intercostal space near the edge of the sternum. It may be heard behind the back of the left shoulder. It is loudest just after the first heart sound, and usually continues through the second sound into diastole. Valsalva's experiment may diminish the diastolic phase. The diastolic part of the murmur is occasionally slight or absent in children. The closure of the pulmonary valves is loud and often palpable. A thrill may be present in half the cases. The enlarged pulmonary artery may cause slight pulsation and an area of dullness near the sternum.

RADIOLOGICAL FINDINGS. The important positive radiological findings are dilatation of the pulmonary artery. But this may be by no means conspicuous (9). The pulmonary arteries tend to be full and may pulsate freely. There may be increase in the pulsation of the ventricles, which may be enlarged; the left auricle may be dilated (10). It may be remarked that none of these findings may be conspicuous and helpful in the clinical diagnosis (Plate 7).

The electrocardiogram is usually normal; occasionally there is right axis deviation. The normal curve is important in confirming the diagnosis and excluding other lesions that may be associated.

The size of the ductus obviously cannot be gauged by the

... LESIONS. Other congenital lesions have been found in two-thirds of all cases (11). We think that those who grow up

are almost always uncomplicated. The commonest association is with pulmonary stenosis; coarctation of the aorta is not infrequent, and may produce a remarkable combination of signs (12). We have noted a patent interventricular septum and another with aortic stenosis. Pulmonary regurgitation may be present if the artery becomes very large. If the enlargement becomes aneurysmal, pressure on the left recurrent nerve may result. The increase of pressure in the pulmonary artery favours the formation of atheroma (2). The ductus may thrombose (13), or thrombosis may arise in the aneurysmal pouch due to its partial obliteration (14). Such a pouch may be revealed by angiocardiography (15). The late filling of the pulmonary artery from the aorta can be demonstrated in this way (28).

INCIDENCE COURSE AND COMPLICATIONS. There were 92 cases in Abbott's series of 1,000. Females were nearly twice as common as males. The average age in one series was twenty-four years (11). Although patients may survive past fifty, it is rare to meet with cases above forty years of age. For a time there was no great disability in many, but their lives were shorter (16). Ultimately heart failure came in about half, the majority dying suddenly. Bacterial infection occurred in about a quarter. The infection starts at the pulmonary end of the ductus, and may arise where the stream impinges on the wall of the pulmonary artery opposite. From here the infection spreads down the artery to the pulmonary valves.

Ligation of the Ductus Arteriosus. The pioneer work of Gross (17) has opened up an important new surgical advance. This is not the place for surgical details. The operation is not unduly severe. Difficulty may arise from thickening of the tissues around the channel, from its size and thin wall, and from its shortness. Past tuberculosis of the glands in the neighbourhood may lead to adhesions. Calcified glands are a warning sign. Probably the approach is easier in children; they are very little affected by the operation. A small pneumothorax may develop at the apex or an effusion at the base (18, 19).

EFFECT OF OPERATION. The heart may decrease in size if previously enlarged. It has been shown that there is a decrease in the kymographic movement of the heart, in the transverse diameter and in the left auricle; in the blood volume, and in the

circulation rate (6). The enlarged pulmonary artery may slowly decrease in size. The typical murmur usually disappears, but a systolic murmur from a dilated pulmonary artery may persist. Perhaps the combination of this with a pulmonary diastolic may account for the apparent persistence of the murmur which has been noted (20), even after ligation and division (21).

In an infected case of ours, where the typical murmur came back, ultimate autopsy showed that the vegetations had prevented complete occlusion, and the pulmonary valves were also incompetent from infection. In one instance (22) a transient renal failure occurred. We have not observed any alteration in renal function in our cases The diastolic pressure tends to rise if it has been low, sometimes considerably. But there are no constant changes.

CONCLUSION In non-infected cases the results are good; sometimes the improvement in the child's health and development are dramatic. When there has been dyspnœa it has been relieved The ductus occasionally appears to recanalize. If it were always possible to divide it as Gross does (23), this would be eliminated. But the technical difficulties are considerable.

In infected cases ligation offers a good chance of saving life, perhaps in two-thirds of cases (16, 24). The use of penicillin has greatly improved the outlook here.

INDICATIONS FOR OPERATION. Ligation of the ductus is clearly indicated as soon as infection is diagnosed (16), and should be combined with penicillin and chemotherapy. The dosage may need to be up to three mega units daily of penicillin. X-ray examination of the lungs may show infarcts confirming diagnosis of infection (8). Another indication would be "circulatory embarrassment" (25) With this one would agree. This is likely to be an indication in older patients (8). How far ligation is prophylactic against infection one cannot yet say. It should reduce the incidence. In our opinion the operation should be done in any child, particularly if it is weedy or ill grown (9). We have noted rapid improvement in several subjects between the ages of ten and sixteen years. Apart from this, the curing of an abnormality which, though it may not be a cause for some time of much disability, certainly does shorten life, and will deter from many sorts of employment and activity, and from life assurance, is surely worth while. The operative risk is small in skilled hands We

would advise it for all cases, preferably between the ages of six and twenty years (9). In children the ductus is nearer the surface; the patients suffer less from shock (25). As age advances the ductus becomes shorter (26). The psychological effect of cure and eliminating restrictions, so that the patient feels no longer different from the rest, is enormous.

It is necessary to decide whether other lesions are present; there should not be great difficulty in this; pulmonary stenosis will be shown by its own murmur and thrill lower down; the pulmonary second sound may be weak or wanting, the cardiogram will show clear right axis deviation. Coarctation may be obvious if at all severe. These lesions contra-indicate ligation. A patent interventricular septum should not debar; nor an aortic lesion.

REFERENCES

1 Christie (1930) *Amer J Child Dis*, **40**, 323
2 Gross, R E (1939) *Ann Surg* **110**, 321
3 Barclay *et al* (1938) *Brit J Radiol*, **11**, 570
4 Kennedy, Clark (1942) *Amer J Physiol*, **136**, 140
5 Brown (1939) *Congenital Heart Disease* London
6 Eppinger, Burwell, Gross (1941) *J clin Invest*, **20**, 127
7 Eppinger, Burwell (1940) *J Amer Med Assoc*, **195**, 1262
8 Gilchrist (1945) *Brit Heart J*, **7**, 1
9. East (1945) *Brit Heart J* **7**, 95
10 Shapiro, Keys (1943) *Amer J med Sci*, **206** 174
11 Abbott, M E (1936) *Atlas of Congenital Heart Disease*, New York
12 Graham, Kerr (1941) *Brit Heart J*, **3** 121
13 Jager (1940). *Amer Heart J* **20** 236
14 Altschule (1937) *Amer Heart J*, **14**, 113
15 Steinberg *et al* (1943) *Amer J Roentgenol*, **50**, 306
16 Bourne (1945) *Brit Heart J* **7** 91
17 Gross (1939) *New England J Med*, **222**, 510
18. Keele, Tubbs (1940) *St Bart's Hosp Rep* **1**, 175
19. Donovan *et al* (1943) *Amer J Roentgenol* **50** 293
20 Touroff (1940) *J Thoracic Surg*, **10** 59
21. Bourne (1941) *Brit Heart J* **4**, 228
22 Hubbard Emerson, Green (1939) *New Eng J Med* **221**, 481
23 Gross (1944) *Surg Gynec Obst*, **78**, 76
24 Tubbs (1944) *Brit J Surg* **32** 1
25 Hunter (1945) *Brit Med J*, **1** 731
26 Gebauer Nichol (1941) *Ohio State Med J*, **37**, 538
27 Cournand (1947) *Bull New York Acad Med*, **23** 27
28 Chavez, Dorbecker Celis (1947) *Amer Heart J*, **33** 560
29 Porter (1947) *Amer J med Sci*, **213**, 178

Congenital Idiopathic Hypertrophy of the Heart

This group of cases with cardiac enlargement were first called "idiopathic" because no cause was found. Now more and more of them have a definite ætiology.

Von Gierke's Disease. In these cases the heart is enlarged in early infancy. The fibres are large and vacuolated and stains show that they contain excess of glycogen (1). The fibres may appear as hollow cylinders (2) The disease is probably congenital (3), and, as is well known, affects also the liver and kidneys. The heart may be so large as to affect the breathing In spite of the great size, even reaching four or five times the normal, it may still retain a remarkable degree of efficiency (4). Heart failure or intercurrent infection usually brings life to a close in a year or so when the heart is much involved. The other cases live longer.

There is no characteristic cardiogram apart from a tendency to low voltage (5)

In addition to the glycogen storage disease, there are other causes which may give great enlargement of the heart, apparently idiopathic, in early infancy (5):

1. Neoplasms (rhabdomyoma).
2. Abnormalities of the great vessels.
3. Abnormalities in the coronary arteries. These are the cause of great enlargement, particularly if one or both should arise from the pulmonary artery (6). Replacement fibrosis occurs, and the T waves of the cardiogram may be inverted (7). Cardiac aneurysm may develop (8). The collateral circulation through aberrant vessels may, on the other hand, be quite efficient (9).
4. Various forms of myocardial disease, characterised by degeneration and replacement fibrosis. These have cardiograms with low voltage (10). They run a short course and end in failure. The hearts are much enlarged: sometimes the lesions are [illegible]

[illegible] studied, fewer and fewer will deserve that name.

REFERENCES

1. Pompe (1933) *Ann. Anat Path*, 10, 23
2. Antopol Heilbrun [illegible]
3. [illegible] 354
4. [illegible]
5. [illegible]
6. [illegible]
7. [illegible] *J*, 24, 118
8. Barnard (1939) *J Path Bact*, 47, 311
9. King (1940) *Brit Heart J*, 2 79
10. Kugel, Stoloff (1933) *Amer J. Child Dis*, 45, 828
11. Kugel (1939) *Amer Heart J*, 17, 602

Cyanosis in Congenital Disease of the Heart

Cyanosis depends upon the presence in the blood of a degree of oxygen unsaturation that amounts to 6.7 volumes per cent. According to Lundsgaard and van Slyke (1923) there are several causes for cyanosis in congenital lesions of the heart.

A. Primary Factors.

1. (L factor). Insufficient oxygenation in the lungs.
2. (D factor). Increased deoxygenation in the capillaries due to stasis.

B. Secondary Factors.

1. (Alpha factor). Venous-arterial shunt.
2. (T factor). Total hæmoglobin content of the blood.

The "L" factor may arise when the blood is prevented from reaching the lungs. Stasis at the periphery will introduce the "D" factor. The Alpha factor will mean probably that about one-third of the total volume of the blood is shunted from right to left, missing the lungs. It will be seen that in some lesions the tendency to cyanosis will be more severe than in others. For instance, in the tetrad, the patent septum and the dextroposed aorta favour the mixture of venous and arterial blood ("Alpha" factor); the stenosed pulmonary orifice favours the "L" factor. Possibly this latter cause is the more important (9). Failure of the right ventricle will introduce the "D" factor.

A simple pulmonary stenosis may not be enough to raise the "D" factor until the right side fails. The Alpha factor may not be raised until an arterio-venous shunt (as in septal defect, or patent ductus) is reversed.

Exercise often accentuates the causes of cyanosis. In infants it may appear transiently on crying or suckling. Finally, more or less *pari passu* with cyanosis, goes the tendency to compensatory polycythæmia, which increases absolutely the amount of reduced hæmoglobin in circulation ("T" factor). Children can have an oxygen saturation of 65 per cent without polycythæmia (9). Polycythæmia may, by increasing the viscosity of the blood, interfere with oxygenation in the lungs, and so introduce the "L" factor (2).

Tissue Changes. Clubbing of the fingers and of the toes accompanies cyanosis and polycythæmia. The nose and lips may

also appear full. The first changes are seen at the root of the nail, where the sulcus is filled in (3); all stages can be made out up to the typical drumstick. Study of the capillaries shows that the blood flow in them is slowed, for there is dilatation (4). There is an increase in the digital arterial pressure; which raises the flow of blood per unit of surface in the finger bed (5). Clubbing is rarely seen under the age of two years (6).

Severe cyanosis is a sign of the risk of hemiplegia in infants, particularly with the tetrad (7). This is perhaps associated with the increase of viscosity of the blood (8)

REFERENCES

Dextrocardia.

The heart lies on the right side of the chest, with the apex to the right. Strictly speaking, the word should not be used for cases in which the heart is displaced to the right because of pulmonary disease or elevation of the left half of the diaphragm. These types are better described as displacements.

The abnormality must arise very early in fœtal life (1). Cockayne considers that transposition *is* due to the formation of a sinistral instead of a dextral spiral in the viscera. Complete transposition of the viscera is inherited as a recessive character, and is determined by a single autosomal gene

There are t

heart. In this case the arterial ventricle still forms the apex of the heart, but points to *the right* This is the commoner variety. The electrocardiogram is characteristic. Lead I is completely inverted (mirror image), all the deflections pointing downward. Lead II and lead III are transposed, so that lead II is the lead III of the normal curve. A similar electrocardiogram can be obtained

Cyanosis in Congenital Disease of the Heart

Cyanosis depends upon the presence in the blood of a degree of oxygen unsaturation that amounts to 6.7 volumes per cent. According to Lundsgaard and van Slyke (1923) there are several causes for cyanosis in congenital lesions of the heart.

A. Primary Factors.

1. (L factor). Insufficient oxygenation in the lungs.
2. (D factor). Increased deoxygenation in the capillaries due to stasis.

B. Secondary Factors.

1. (Alpha factor) Venous-arterial shunt.
2. (T factor). Total hæmoglobin content of the blood.

The "L" factor may arise when the blood is prevented from reaching the lungs. Stasis at the periphery will introduce the "D" factor. The Alpha factor will mean probably that about one-third of the total volume of the blood is shunted from right to left, missing the lungs. It will be seen that in some lesions the tendency to cyanosis will be more severe than in others. For instance, in the tetrad, the patent septum and the dextroposed aorta favour the mixture of venous and arterial blood ("Alpha" factor); the stenosed pulmonary orifice favours the "L" factor Possibly this latter cause is the more important (9). Failure of the right ventricle will introduce the "D" factor.

A simple pulmonary stenosis may not be enough to raise the "D" factor until the right side fails. The Alpha factor may not be raised until an arterio-venous shunt (as in septal defect, or patent ductus) is reversed.

Exercise often accentuates the causes of cyanosis. In infants it may appear transiently on crying or suckling. Finally, more or less *pari passu* with cyanosis, goes the tendency to compensatory polycythæmia, which increases absolutely the amount of reduced hæmoglobin in circulation ("T" factor). Children can have an oxygen saturation of 65 per cent without polycythæmia (9). Polycythæmia may, by increasing the viscosity of the blood, interfere with oxygenation in the lungs, and so introduce the "L" factor (2).

Tissue Changes. Clubbing of the fingers and of the toes accompanies cyanosis and polycythæmia. The nose and lips may

6 MANCHESTER, WHITE (1938) *Amer Heart J.*, 15, 493
7. LICHTMAN (1931) *Arch int Med*, 48, 683
8 STEVENSON (1937) *Quart J. Med*, 24, 395
9 TORGACS (1947) *Brit Heart J*, 9, 27

Abnormalities of the Coronary Arteries

The coronary arteries start to develop about the end of the second week of fœtal life, before the truncus arteriosus is divided by the spiral septum If, when the truncus is divided into the pulmonary artery and aorta, the buds forming the coronary arteries lie in front of the septum, they will be found to arise from the pulmonary artery.

The left coronary artery is more usually misplaced and may arise from the pulmonary artery. The supply of venous blood causes degeneration and fibrosis and calcification in the myocardium (1) Considerable enlargement of the heart, with gallop rhythm, may result (2) The cardiogram may be abnormal, both in QRS and T waves. The conclusion is that the supply of venous blood at low pressure causes the ischæmic changes in the muscle (3). Patients with this defect do not live long.

While ill effects result from the origin of the left coronary artery from the pulmonary artery if the collateral circulation is not good, the results in other cases may not be so unfavourable. The origin of the right coronary artery from the pulmonary artery is not incompatible with health and survival (4)

These cases may resemble congenital idiopathic hypertrophy.

A single coronary artery may arise from the aorta. This may be either the left or the right. In one case, for example, the right supplied most of the heart, with a small branch round the front of the pulmonary artery to the left (5). This abnormality in itself does not matter. Perhaps later on the development of coronary disease may have more serious consequences, as in the case of Dr. Thomas Arnold, of Rugby, described by Latham many years ago, in his "Lectures on the Heart."

Absence of the left coronary artery seems to be associated with much ischæmic change in the muscle, and infarction, if it does occur, is extensive (6).

REFERENCES

1 KAUNITZ (1947) *Amer Heart J*, 33 182
2 BROWN (1939) *Congenital Heart Disease,*

in a normal person by interchanging the wires to the right and left hands. Similarly, a normal curve can be obtained by this procedure in a case of dextrocardia. When other congenital defects are present this typical curve may be modified (3).

The skiagram is a mirror picture. The stomach lies to the right, and the liver to the left.

Angina pectoris has been described in dextrocardia with radiation of the pain to the right arm (4). A similar distribution of the pain was noted in a case of coronary thrombosis (5). The electrocardiogram showed the characteristic changes due to posterior infarction modified by those of dextrocardia, exactly as one would expect. In another case of anterior infarction similar findings were noted (6).

Clinically, this form of dextrocardia in itself causes no disability

(ii) Isolated, uncomplicated dextrocardia, without transposition of the viscera (7).

a. The arrangement is the same as in total transposition with inversion of the heart chambers, the right ventricle lying in front and the left behind. The electrocardiogram shows the usual "mirror image" changes. The aorta may be right-sided. The abnormality is of no importance in itself (8) if there are not other abnormalities. But there are more usually other lesions, causing cyanosis; then the condition is said to be "complicated."

b. Heart chambers not inverted.

Here the venous ventricle, lying behind, forms the apex of the heart, and the arterial ventricle lies in front. No "mirror image" is therefore present. The abnormality probably rises later in intra-uterine life than the other.

Other abnormalities, such as pulmonary stenosis and patency of the septa, are frequently seen in these cases. The electrocardiogram will not show the changes due to "mirror image" The associated lesions may cause serious disability.

Isolated inversion of the abdominal viscera may be associated with congenital cardiac defects (9).

REFERENCES

1 COCKAYNE (1938) *Quart J Med*, 27, 479
2. KOSSMAN (1940) *Amer Heart J*, 20, 322
3 RICHARDSON (1942) *Brit Heart J*, 6, 80
4 CAIN, J. C. (1945) *Amer Heart J*, 30, 202
5 CRAWFORD, WARREN (1938) *Amer Heart J*, 15, 240

CHAPTER II

INFECTIONS OF THE HEART, AORTA AND PERICARDIAL SAC

Rheumatic Heart Disease
Libman-Sacks Disease
Subacute Infective Endocarditis
Cardiovascular Syphilis
Diseases of the Pericardial Sac

In this chapter it is convenient to consider together various topics which are often discussed apart. But although ætiology differs on anatomical and pathological grounds, from a clinical point of view they have a great deal in common. Rheumatic heart disease affects all tissues of the heart; there is a close link between the incidence of infective endocarditis and rheumatism, although the former is mainly confined to the valves. The aortic lesions of syphilis and rheumatism have a good deal in common. Libman-Sacks disease has much in common with rheumatic disease. Some phases of rheumatic pericarditis are similar to those of other origin. To diminish entities rather than multiply them, as William of Occam laid down, facilitates understanding.

RHEUMATIC HEART DISEASE

Probably the most interesting new advance on the subject of acute rheumatism concerns its possible cause by streptococcal infection and treatment from this angle.

Ætiology

The Streptococcus. There is now a great deal of evidence that infection of the throat by a group *A* hæmolytic streptococcus precedes the manifestation of rheumatism in many cases. In one epidemic of streptococcal throat infections among rheumatic children, relapses of rheumatism occurred one to three weeks after

3 BLAND *et al.* (1933). *Amer. Heart J*, 8, 787
4 SOLOFF (1942). *Amer Heart J*, 24, 118
5. KING (1940), *Brit. Heart J*, 2, 79
6 ROBERTS, LOUBE (1947) *Amer Heart J.*, 34, 188

Dilatation of the Pulmonary Artery

This is a very rare congenital abnormality when it occurs alone. Great enlargement may be met with in cases of patent atrial septum, patent ductus arteriosus, and the Eisenmenger complex. The whole pulmonary tree may be dilated, the aorta may be hypoplastic. There must be no disease of the lungs or obliteration of the arterioles (1). There will be a systolic murmur, thrill and pulsation over the pulmonary artery. Exclusion of the possible associated lesions is difficult. The thin-walled dilated vessel may ultimately rupture (2). The valves may be bicuspid. Incompetence may occur.

REFERENCES

1 GOLD (1946) *Arch int Med*, 78, 197
2 WILKINSON (1940) *Brit Heart J*, 2, 255

REFERENCES

1 Sheldon (1931) *Lancet*, 1, 1337
2 Coburn, Pauli (1939) *J. clin Invest*, 18, 141
3 Coburn (1936) *Lancet*, 2, 1025
4 Coburn (1935) *J. clin Invest*, 14, 383
5 Homer, Swift (1936) *J Lab clin Med*, 21, 551
6 Green (1942) *Ann rheumat Dis*, 3, 1.
7 Green (1939) *J R Naval Med Serv*, 25, 218
8 Collis (1939) *Lancet*, 2, 817
9 Wilson, Schweitzer (1937). *J. clin. Invest*, 16, 559
10 Schlesinger, Signy, Amies (1935) *Lancet*, 1, 1145
11 Eagles, Fisher, Evans Keith (1937) *Lancet*, 2, 421
12 Eagles, Bradley (1939) *Quart J Med*, 8, 173

Morbid Anatomy. A minute nodule, first described by Aschoff, is the specific lesion of rheumatic fever. A small area of necrosis is the initial change, and around it collect lymphocytes and longer oval cells, the histiocytes. Nodules appear in connective tissue, near a small vessel, later they are invaded by fibrous tissue. They are particularly numerous in the interventricular septum, and under the endocardium and pericardium. It is not uncommon to find an area under the endocardium of the left auricle just above the posterior cusp of the mitral valve (MacCallum's patch)

Valvulitis. In the valves the Aschoff nodule lies under the endocardium, which becomes swollen above it. On this area are deposited the small warty vegetations consisting of platelet thrombi They appear just above the free edges of the valves where they are driven together in closure. Mechanical *trauma* then plays a part in the development of these outward signs of an inward inflammatory process which really *involves* the whole valve (1) Healing then takes place and the vegetations are absorbed, leaving a thickened ridge. New vessels are formed and the valve becomes fibrous. This process repeated again and again, gives rise to the stiff, thick valves of long-standing rheumatic endocarditis.

The mitral valve was always found to be diseased in patients dying of rheumatic carditis. The aortic valves were affected in about half, and the tricuspid valves in about *one-third* (1).

Pericarditis. This is almost invariably present in patients [illegible] ... ises between ten and twenty [illegible] ... between twenty and thirty [illegible] ... *fibrinous* in type, effusions of any size being rare; they may be hæmorrhagic. The histological appearance resembles those of the myocardium and endocardium There is

the attack (1). Further work has shown that infection with streptococci in the throat causes the production of various antibodies in the blood. These are specific, and include precipitins, agglutinins, anti-hæmolysins (2). The titre of these antibodies rose steadily and persistently in rheumatic subjects. The response in the development of the immune response in rheumatic subjects might be delayed in the onset, but persisted longer than in normals. From this it might be inferred that the rheumatic subject deals with the product of streptococcal infection in an abnormal way (3). Some substance may be released in rheumatism which modifies the mesodermal structures. This release may occur when there is immune response to the hæmolytic streptococcus (4). The response causes damage to mesenchymal ground substance with hyperplasia and proliferation of primitive cells (5). Sensitisation may occur, and if organisms survive the delayed immune response, a further release of antigen from them may provoke the inflammatory reaction in the tissues (6).

It would appear that with special technique and precautions, hæmolytic streptococci can be cultured from many sites, notably the heart valves (7) (8). The case against the hæmolytic streptococcus is very strong, but the reason for the reaction to it which is peculiar to the rheumatic subject is still obscure.

Associated Causes. It has long been known that climatic and environmental factors are important in causing rheumatism. The disease is commoner in large towns and wet climates There are the social causes which operate "in poverty, hunger and dirt." Poverty, which introduces the possibilities of malnutrition, bad clothing, and exposure to cold and damp, and fatigue, plays a large part. The disease affects the young. Familial incidence is often conspicuous, and heredity may be important. It has been suggested that the mechanism involved was a single autosomal recessive gene (9).

The Virus Hypothesis. Particles have been found in the pericardial fluid which may be elementary bodies (10). Agglutination reactions on these bodies were, however, somewhat erratic (11). Further agglutination tests showed that many varieties of sera reacted with them. How far a virus may play a part in acute rheumatism is still uncertain; but little further evidence has accrued.

REFERENCES

'67.

074

Clinical Features. The clinical signs of rheumatic carditis depend on the severity of the invasion In the most severe cases the heart is overwhelmed. The child will have fever, tachycardia and pericarditis, and die of general toxæmia. This type of infection is fortunately uncommon, amounting to only 5 per cent of all cases (1) When failure comes on, it tends to be "right ventricular" in type from the start. There is puffiness of the face and the weight increases unexpectedly. Right axis deviation may appear in the cardiogram, with return to normal on recovery. The venous pressure rises rapidly and the liver becomes engorged (2). A gallop rhythm may be heard. Moderately severe cases have fever and tachycardia and pericarditis, with less general constitutional disturbance. Pulmonary lesions may develop at the base of the left lung Arthritis and crops of nodules furnish additional evidence of rheumatism. Erythema marginatum and purpura are not uncommon. The heart enlarges and the apex beat may move out as much as two inches to the left, for the ventricles become dilated. This myocardial weakness is out of all proportion to the prevalence of the Aschoff's bodies. A systolic murmur is audible at the apex. In the early stages this is due to relaxation of the mitral ring With recovery it may disappear. In other cases the murmur in course of time becomes harsher and is heard out in the axilla. The second sound may appear to become reduplicated, and the new sound develops into an early diastolic murmur. These are the cases that are likely to develop mitral stenosis later

It is important to remember that carditis may exist with but few of these manifestations. A persistent tachycardia in a child, for which no other cause can be found, should suggest carditis. Observation of a raised sleeping pulse rate is very important. The rapid rate of an excitable child settles during sleep.

LATENT TYPE. In many cases the constitutional disturbances are slight. The child is listless and pale and loses its appetite. There may be failure to gain weight, or loss of weight. Transient

a fibrinous exudate overlying connective tissue proliferation, with fibroblasts and new vessels and Aschoff's bodies.

The parietal pericardium becomes very thick, and adhesions may extend outside it. Dense adhesions ultimately bind it to the surface of the heart. Pick's syndrome, however, does not result from this inflammation (2).

The lesions of acute rheumatism are widespread. The characteristic histological changes are seen in the subcutaneous *nodules and around the joints. The aorta may show areas of* subendothelial inflammation. The same lesions may be found in the pulmonary artery. The lesions of the brain cause chorea.

PULMONARY LESIONS. A form of pneumonia has been described (3). A fibrinous alveolitis is said to be the conspicuous feature, in which the alveolar ducts become lined with hyaline "membrane." There is later mononuclear infiltration and copious albuminous exudate. The lungs are dark and solid. It is doubtful how far this lesion is specific for rheumatism. Other observers have failed to find specific Aschoff bodies. They consider that the changes are the result of capillary damage, similar to that in other parts of the body (4)

There is no doubt that in acute pericarditis the base of the left lung often becomes inhibited in expansion, and airless, and dull. Distant tubular breathing may be heard. The right side may be affected as well The embarrassment to respiration may become severe if the patient is kept lying flat, and the signs diminish if he sits propped up. One would infer from the rapidity with which these changes may come and go that massive collapse plays an important part in their production; and that lying flat is a bad posture for the patient with acute pericarditis. He should be well propped up.

Search for the stigmata of rheumatism in hearts considered to be free from rheumatic infection showed that they were actually very common. These were usually near the base of the mitral valve. The signs taken as indicative of past rheumatism were arteritis, fibrinoid changes, changes in the elastic tissue, Aschoff's bodies and histiocyte infiltration (5). The prevalence of those lesions, if indeed they are rheumatic in origin, suggests that some form of rheumatic reaction is far from rare, but that most people are sufficiently immune to prevent the development of valvular lesions.

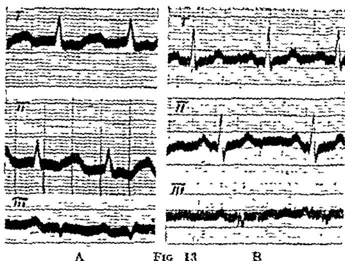
REFERENCES

1 COOMBS (1924) *Rheumatic Heart Disease*
2 JONES, BLAND (1942). *Tr Assoc Amer. Phys*, 57, 267
3 HADFIELD (1938) *Lancet*, 2, 710
4 EPSTEIN GREENSPAN (1941) *Arch int. Med*, 68, 1074.
5 HALL, ANDERSON (1943) *Amer. Heart J*, 25, 64

Clinical Features. The clinical signs of rheumatic carditis depend on the severity of the invasion. In the most severe cases the heart is overwhelmed. The child will have fever, tachycardia and pericarditis, and die of general toxæmia This type of infection is fortunately uncommon, amounting to only 5 per cent of all cases (1) When failure comes on, it tends to be "right ventricular" in type from the start There is puffiness of the face and the weight increases unexpectedly. Right axis deviation may appear in the cardiogram, with return to normal on recovery. The venous pressure rises rapidly and the liver becomes engorged (2). A gallop rhythm may be heard. Moderately severe cases have fever and tachycardia and pericarditis, with less general constitutional disturbance. Pulmonary lesions may develop at the base of the left lung. Arthritis and crops of nodules furnish additional evidence of rheumatism. Erythema marginatum and purpura are not uncommon The heart enlarges and the apex beat may move out as much as two inches to the left, for the ventricles become dilated. This myocardial weakness is out of all proportion to the prevalence of the Aschoff's bodies. A systolic murmur is audible at the apex. In the early stages this is due to relaxation of the mitral ring. With recovery it may disappear. In other cases the murmur in course of time becomes harsher and is heard out in the axilla. The second sound may appear to become reduplicated, and the new sound develops into an early diastolic murmur. These are the cases that are likely to develop mitral stenosis later

It is important to remember that carditis may exist with but few of these manifestations. A persistent tachycardia in a child, for which no other cause can be found, should suggest carditis. Observation of a raised sleeping pulse rate is very important. The rapid rate of an excitable child settles during sleep.

LATENT TYPE. In many cases the constitutional disturbances are slight. The child is listless and pale and loses its appetite. There may be failure to gain weight, or loss of weight. Transient



A Fig 13 B

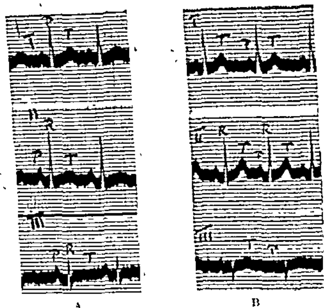
A —Rheumatic carditis Note prolongation of P-R interval, merging P with preceding T, and slurring of ventricular complex

B —From the same case Return to normal some months later

pains in the limbs may have been noted. There may, however be a raised sedimentation rate, which may persist for a long time (3). There may be no fever, no arthritis and no nodules (although even one only will be diagnostic of active disease). The heart, however, shows slight enlargement, with a well developed apical systolic murmur The heart has received permanent damage with but few distinctive signs

ELECTROCARDIOGRAMS HEART BLOCK. There are two possible causes. It has been shown that in some cases the delay in conduction may be temporarily abolished by atropine (4) It may therefore be concluded that the prolongation of the conduction in these cases was due to increase in vagal tone (5). In a few cases the block is permanent and not changed by atropine. It has been found that there may be lesions of the collagen fibres in the upper part of the septum These may enclose and compress the bundle when they become swollen (6)

Pressure on the carotid sinus increases the block when there is active disease, particularly when the P-R interval is about 0.18 to 0.20 second In normal persons this increase does not occur. This reaction may be evidence of active disease (7). (Fig. 13, a and b.)



A B

FIG 14

A—Rheumatic carditis From a child of ten with pains and slight cardiac enlargement Note small T-waves
B—Note larger T-waves seven weeks later

Extrasystoles may be noted, frequently auricular in origin. There may be depression of the S-T interval. The curves of pericarditis are described elsewhere (p. 87). There may be flattening of the T-waves. (Fig. 14, a and b.)

These changes are not common in children who are well enough to be up and about. There may be prolongation of systole in acute carditis, as is shown by measurement of the Q-T time (13).

It is suggested that hypertrophy of the left ventricle rather than of the right may account for some of the changes found in precordial leads The ordinary standard leads may be quite misleading. Confirmation by autopsy is needed to settle the matter (14)

Prognosis. The survival rate was investigated by Coombs, who followed a large number of cases over a long period (1).

Of those with definite signs of carditis, one-quarter recover completely. Though exceptions occur, the signs will usually disappear in these cases within one year.

Including only those with definite signs of carditis.	*Including also all suspicious cases.*
5 per cent did not survive one year.	
22 per cent died before the age of twenty.	19 per cent died before twenty.
42 per cent survived with damaged hearts.	37 per cent survived with damaged hearts.
31 per cent recovered completely.	44 per cent recovered.

In another series of 175 patients, 50 per cent sustained no permanent cardiac damage. If valvular lesions did not develop in the first attack *they were unlikely to do so later on in spite of* further attacks (8).

Twenty-two per cent do not survive to adult life. The average age of onset in this series was 10 years, so that these patients lived less than 10 years from their first attack. They form a group for whom little can be done. For some reason they are peculiarly susceptible to infection with rheumatism They go downhill *through a series of reinfections. Surmounting the first attack of* carditis, they are left with a lesion of the mitral valve. After a year or two they have a second attack. This may betray itself by tonsillitis, or by fever, or arthritis and subcutaneous nodules. Or the only sign may be that the aortic valve is now incompetent. Alternatively the first or second attacks may leave pericardial adhesions, and the heart may slowly but steadily increase in size. *Finally, they succumb to an infection they can no longer resist,* and a prolonged bout of fever leads to death Or later on at puberty auricular fibrillation sets in, and they die with all the signs of circulatory failure. The process in these cases has been well named "malignant rheumatic carditis" (9)

It seems clear that progressive cardiac enlargement is always a bad sign. The mortality is higher than when enlargement is absent, or *when the degree of enlargement remains stationary (10).*

POLYARTERITIS NODOSA. Cases have been recorded where the lesions of polyarteritis *nodosa were combined with those of* rheumatism (11). The patients had polyarthritis, endocarditis

and fever. There was a history of scarlet fever in two. While under observation they had severe abdominal pain, and purpura After death, Aschoff's bodies were found in the heart, as well as the typical lesions of polyarteritis in the arteries of the heart, kidneys, and abdominal viscera.

The abdominal pain was sufficiently severe to lead to laparotomy in two instances Abdominal pain is sometimes met in carditis. In Henoch's purpura it is associated with purpuric eruptions. In those cases who do not respond to salicylates, the possibility of a polyarteritis nodosa should be borne in mind.

It would appear that when carditis occurs in children either alone or with subcutaneous nodules, it is more likely to cause permanent damage, than when polyarthritis is a conspicuous feature. Chorea is less usually followed by carditis. In adults the first attack of polyarthritis is less often followed by carditis than in children. In adults serious damage from an initial attack of carditis is also less probable than in younger patients (12).

REFERENCES

1 COOMBS, CAREY (1924) *"Rheumatic Heart Disease,"* Bristol
2 [illegible] ., 61, 1003
3
4
5
6
7 [illegible] *J med Sci* 209, 409
8 [illegible] 23, 242
9
10 [illegible] *J*, 21 440
11 [illegible] *Arch Int, Med*, 54, 170
12 DE LICE, DODGE MCEWEN (1942) *Amer Heart J*, 26, 681.
13 TARAN, SZILAGYI (1947) *Amer Heart J*, 33, 14
14 FIRST *et al* (1947) *Amer Heart J*, 33, 1

Treatment. REST. The essence of treatment is prolonged rest. The child should be confined altogether to bed, and should rest on one pillow, unless this *position* is uncomfortable [illegible]
presence of [illegible]
of the lung [illegible]
child shou [illegible] as necessary [illegible]
maintained [illegible]
The s [illegible]
The s [illegible]
[illegible] returned to normal

SALICYLATES. *Sodium Salicylate.* For nearly sixty years at least, large doses of sodium salicylate, 120 to 160 grains daily, have been recommended for acute rheumatic fever. As it is now possible to estimate the level of salicylates in the blood, interest in this topic has revived. The optimum level is about 35 to 40 mg. per cent. This is achieved in an adult by 10 grammes (150 grains) daily (1). Another method of dosage is to give 1½ grains per pound of body weight daily. The drug has been given intravenously, 1 grain per pound in a 1 per cent solution at six-hour intervals for six days. There is thereby serious risk of severe toxic effects. These may be hypothrombinæmia and diminished coagulability of the blood (2) This method has nothing to recommend it. It is doubtful whether there is any protection gained against cardiac complications. The fever and arthritis are, of course, controlled, as has long been known. Some prefer aspirin, 30 to 60 grains daily, often in the form of calcium aspirin.

Convalescence. A prolonged convalescence is necessary. Iron may be needed for anæmia. A special heart home is a great advantage, for education can be continued, and a child with a rheumatic heart does better with other children suffering from the same disability as herself.

After Care. Schooling must not be neglected. Special care should be taken to guard a rheumatic child against chills. Changing of wet boots should be enforced rigorously; woollen stockings should be worn. The value of tonsillectomy has been the subject of discussion. It is not safe to remove tonsils while there is any activity of the rheumatic infection. The absence of tonsils does not provide any safeguard against the child having sore throats due to infection of the nasopharynx with hæmolytic streptococci. Some have thought that enucleation of the tonsils does not diminish the frequency of subsequent carditis (3), but the presence of already septic tonsils must make the child more liable to infection, and reinfection is the chief danger. It is wise, therefore, to remove septic tonsils during a period of quiescence (4).

PROPHYLACTIC TREATMENT. This may be considered under two headings. There are the general health measures without which individual steps are of but little avail. There is no doubt whatever that in order to reduce the incidence of rheumatism the evils of bad housing, and under nutrition must be eliminated so that the

environmental causes which seem to determine the reaction of the individual to the ubiquitous hæmolytic streptococcus are minimised. This will be more effective than individual prophylaxis against a streptococcal throat infection.

Sulphonamides. A good deal has been attempted by giving prolonged prophylactic courses of sulphanilamide to rheumatic children. In one series, 1 to 2 grammes of sulphanilamide was given daily through winter and spring. In the controls there were 39 per cent of infections with hæmolytic streptococci, with 10 per cent of major rheumatic complications. Among the treated there were 2.7 per cent of infections and 1.1 per cent developed sequelæ (5) In another series 815 patients were treated; 1 to 1.2 gramme of sulphanilamide was given daily. There were no major rheumatic attacks among those treated, but 15 occurred among controls (6). In another clinic there were 18 infections among 30 patients, of whom 14 developed rheumatic sequelæ. Only 1 out of 54 treated with sulphanilamide developed an uncomplicated infection (7). In a summary of the four clinics there were recurrences of rheumatism in 6 out of 352 treated cases, while there were 77 among 350 untreated controls (8).

Sulphadiazine has also been used in doses of 1 gramme daily. There was 15 per cent of mild reactions (9). In another series 35 per cent showed reactions with this drug, 1 gramme daily being given. Sulphathiazole caused reactions in 5 per cent (10); 0.5 gramme was given daily for 1 to 2 years.

On the whole, the toxic reactions are likely to occur, if at all, early in the course. The patients must be watched carefully, and examined from time to time for albuminuria and leucopenia. Patients are warned to report any rash, and to discontinue the drug if any febrile illness, or sore throat occurs The treatment should continue at least all the winter, and some suggest all the year round.

Salicylates. In a series of 186 cases, 4 to 6 grammes (60 to 90 grains) of sodium salicylate were given daily for some months. One rheumatic attack occurred among the 47 treated cases, and 57 developed among 149 untreated patients. It was noted that there was no modification of the anti-streptolysin titre (11).

These figures for sulphonamides and salicylates are impressive, and further results over longer periods of time will be awaited with

interest. If the patients can be relied on to take the drug regularly and there is adequate observation, the risk of untoward reactions is not large, and the prospects of benefit are considerable. It remains to be seen whether the treatment is really practicable.

REFERENCES

1 COBURN (1943) *Bull Johns Hopkins Hosp*, 73, 435
2 [illegible] (1945) *[illegible] J Pediat*, 27, 59.
3 [illegible] 1, 61
4 [illegible]
5 [illegible] *Pediat*, 24, 483
6 [illegible] 126, 490
7 [illegible]
8. [illegible] *[illegible]er. J Child. Dis*, 64, 693.
9. [illegible] *[illegible]d Assoc*, 126, 88
10. [illegible] *[illegible]at*, 27, 516.
11 [illegible] [illegible]5, 180

Chronic Rheumatic Heart Disease. About one-quarter of all cases of rheumatic heart disease in adults have no recollection of any acute attack during childhood. In them the original infection was latent. It was insufficient to cause signs or symptoms, but sufficient to start the cicatrising process which leads to valvular inefficiency.

The use of the term "chronic rheumatic heart disease" is in a sense misleading, since reinfection continues to recur. In a study of 160 necropsies *criteria of activity were found in the following* proportions among the different age groups. In those dying up to the age of 20, signs of activity were present in practically all. In the 46 cases dying between 10 and 50 years, 40 per cent had active lesions; 28 cases passed the age of 50, one of whom lived to 80 with a mitral and aortic stenosis In them, hypertension, atheroma and emphysema played a part, and only 10 per cent had any sign of activity. The conclusion is that, up to 50 years of age, deaths in rheumatic heart disease from circulatory failure are due to reinfection rather than to the mechanical stress of the valvular lesion (1).

Mitral Stenosis. *The mitral valve is nearly always diseased* in rheumatic hearts. Pure mitral stenosis is found in women thrice as *often* as in men. This may be *due to the high incidence of* chorea in girls; it is not uncommon to meet mitral stenosis with a history of chorea years before in childhood.

The physical sign of mitral stenosis is the diastolic murmur.



PLATE 9

Mitral Stenosis and Auricular Fibrillation.

Note prominence of pulmonary artery and conus of right ventricle.

It may be short in presystole or it may be signalised by a long diastolic rumble. The murmur is not represented as being truly crescendo in sound records. This is an auditory illusion due to the fact that the murmur ends in a loud first sound, of an abrupt accentuated character. When the murmur is very short this type of sound should give warning of the possibility of its presence and suggest careful search It is easily missed owing to its local character. In a doubtful case it may be elicited by auscultating with the patient in the left lateral position, particularly when the heart rate has been accelerated by exercise. Delay in auriculo-ventricular conduction may place the murmur in mid-diastole.

Auricular fibrillation will abolish the presystolic murmur (auricular systolic), any mid-diastolic element persisting. In young patients with carditis the first indication of mitral stenosis is an early diastolic murmur. The apex beat is slapping and staccato

Evidence of the increase in pulmonary pressure is given by the accentuated pulmonary second sound This has been confirmed by the intracardiac catheter (5). On screening, the shadow of the pulmonary artery and its left branch is enlarged and below it can be seen the bulge of the shadow of the hypertrophied conus of the right ventricle (Plate 9). Most important of all is the enlargement of the left auricle (Plate 10), seen in the right anterior oblique position projecting back in the upper two-thirds of the retrocardiac space (see Plate 10). Barium in the œsophagus helps to delineate the border of this shadow. There are shadows of general engorgement of the pulmonary circulation (Plate 11).

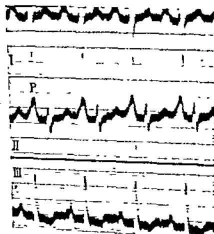


Fig 15
Large P-waves in mitral stenosis. Right axis deviation

Cardiograms. These show large P waves, especially in leads II and III and right axis deviation (Fig. 15), though with lesser

degrees of stenosis the curve may be normal. In advanced cases the curve shows right ventricular hypertrophy (Fig. 16).

The special effects of mitral stenosis are the liability to auricular fibrillation sooner or later, and the increase in pressure in the pulmonary circulation.

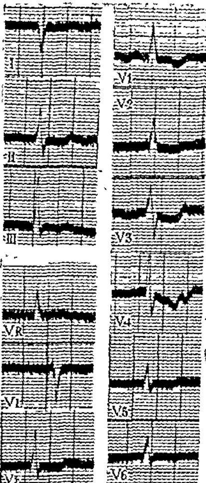


FIG 16

Right ventricular hypertrophy in mitral stenosis Auricular fibrillation · Chest leads show large R waves in V_1 and V_2 T is negative from V_1 to V_5 The heart is vertical

Mitral Regurgitation. In some cases of mitral disease only a persistent harsh systolic apical murmur is heard. This sound must be produced by reflux into the auricle. But the pathological basis of this murmur is still in some dispute. The valves are presumably abnormal. From the evidence of phonocardiograms, it has been suggested that the systolic murmur, when no presystolic is heard, is due to auricular systole and should be regarded as evidence of mitral stenosis (21). It may be safer at present to keep to a pathological change and use the term 'mitral disease' (2)

RUPTURE OF CHORDÆ TENDINEÆ. Apart from the destructive effect of bacterial endocarditis, the lesion may occur in many rheumatic valves. The rupture allows free regurgitation into the auricle and is marked by the appearance of a loud systolic murmur and sometimes a thrill at the apex. Heart failure may develop rapidly, or its onset may be insidious. But in some cases the onset is delayed for months or years (3).

Rupture of a papillary muscle, which may result from trauma, causes similar signs, but rapid failure with acute pulmonary



PLATE 11

Mitral Stenosis.

Engorgement of pulmonary veins.

degrees of stenosis the curve may be normal. In advanced cases the curve shows right ventricular hypertrophy (Fig. 16).

The special effects of mitral stenosis are the liability to auricular fibrillation sooner or later, and the increase in pressure in the pulmonary circulation.

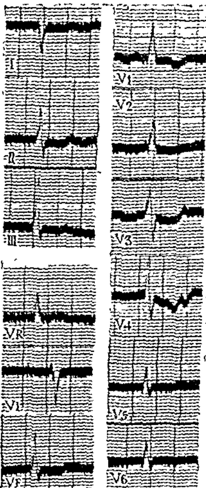


Fig 16

Right ventricular hypertrophy in mitral stenosis Auricular fibrillation · Chest leads show large R waves in V_1 and V_2 T is negative from V_1 to V_5 The heart is vertical

Mitral Regurgitation. In some cases of mitral disease only a persistent harsh systolic apical murmur is heard. This sound must be produced by reflux into the auricle But the pathological basis of this murmur is still in some dispute. The valves are presumably abnormal. From the evidence of phonocardiograms, it has been suggested that the systolic murmur, when no presystolic is heard, is due to auricular systole and should be regarded as evidence of mitral stenosis (21). It may be safer at present to keep to a pathological change and use the term 'mitral disease' (2)

RUPTURE OF CHORDÆ TENDINEÆ. Apart from the destructive effect of bacterial endocarditis, the lesion may occur in many rheumatic valves. The rupture allows free regurgitation into the auricle and is marked by the appearance of a loud systolic murmur and sometimes a thrill at the apex. Heart failure may develop rapidly, or its onset may be insidious. But in some cases the onset is delayed for months or years (3).

Rupture of a papillary muscle, which may result from trauma, causes similar signs, but rapid failure with acute pulmonary



PLATE II

Mitral Stenosis.

Engorgement of pulmonary veins.

To face p. 58



PLATE 12

Mitral Stenosis. Great enlargement of the left auricle.

œdema is almost invariable, particularly if myocardial infarction has led to it.

Apart from these causes, mitral reflux will be found as a result of incompetent valves in grossly dilated left ventricles, such as occur in hypertensive patients, or in those with aortic reflux of syphilitic origin; or when an infarct has caused damage to a papillary muscle so that it atrophies.

CALCIFICATION OF THE MITRAL VALVE. This occurs in the flaps or at the base of the cusps. Rheumatic infection usually precedes it (18). It may not infrequently be found in old people at the base of the mitral valve in the annulus fibrosus. A loud and harsh systolic murmur may be heard. It may have caused no signs or symptoms at all, only being found at autopsy. Examination of the specimen by X-rays shows the calcification well (10). In the skiagram the calcified tissue may be seen (4). On screening, the valves may be seen to move towards the apex at ventricular systole (20).

PULMONARY ARTERY. Atheromatous degeneration may be found both in the trunk and also in the main branches, presumably following the increased pulmonary pressure, which may reach a high level. Normally the right ventricular systolic pressure, estimated by intra-cardiac catheter, averages 25 mm. Hg. This gives the pressure of the pulmonary artery. In mitral stenosis the average was 41 mm Hg.: when there was failure it rose to 103 mm. Hg. (5) There is no wonder that the thin-walled artery dilates and that the pulmonary valves become incompetent, so that the Graham Steell murmur is heard.

HARMLESS MURMURS. At the apex soft systolic murmurs are often heard in persons thought to be healthy. One must exclude the murmur that may mean the onset of endocarditis in patients with active rheumatism. If the heart is normal in size, vague systolic murmurs at the apex or base are of no account. Such murmurs may be hæmic or exocardial. The hæmic murmur is usually found with anæmia, but it may be present apart from this, particularly at the base of the heart. It is soft, blowing, and vague in localisation and conduction It often varies

of the heart, usually on the left. They depend for their origin upon the interruption of the filling of the lungs with air by the movements of the heart. They are usually related to a particular phase of respiration, especially inspiration. They are sometimes very obviously an interrupted breath sound. Holding the breath, especially in expiration, abolishes them. Indefinite murmurs of this nature should always be investigated with the patient recumbent and standing. The site and extent of maximum intensity should be noted. Some are best heard between the apex and the sternum, and tend to spread towards the pulmonary area. There is one type, rather louder and coarser than the others, which is heard late in systole, following the first sound by an interval and running into the second sound. Its causation is obscure; it is not associated with any other abnormality and remains unchanged for years. It is no doubt harmless. The error it occasions is to mistake it for a presystolic murmur by taking the second sound for the first, and diagnosing mitral stenosis. Similarly, mitral stenosis may be erroneously diagnosed when an innocent apical systolic murmur is found in a nervous young adult with a loud mitral first sound and a third sound early in diastole. This is a common clinical combination, conspicuous when the patient lies on his left side.

It has been suggested that here the normal mitral opening is relatively too small for the rush of blood and so in a sense relatively stenosed; hence the signs (6). It seems more likely that the third sound is due to vibration set up in the wall of the empty ventricle by the inrush of blood early in diastole.

CYANOSIS is apt to occur early in mitral disease. There appears to be an increase in the peripheral utilisation of oxygen, due to a slower flow of blood; cyanosis is then of peripheral origin. There is in some cases a decrease in the oxygen saturation of the arterial blood, the result, perhaps, of changes in the walls of the pulmonary alveoli. It has been suggested that there may be slight obstruction to the superior vena cava by some obstacle which the passage of a cardiac catheter reveals, possibly the large left auricle. This has been held to account for the cyanosis peculiar to the mitral facies (7).

HÆMOPTYSIS is quite a common occurrence. There are several possible causes. There may be emboli causing infarction

Paroxysmal hæmorrhages may occur in young patients, with attacks of profuse bleeding lasting several days. The skiagrams of the lungs show a general loss of translucency similar to that seen in pneumonia (8)

The mechanism may be due to increase of pressure on exertion from a strongly acting right ventricle. This acts on sclerosed pulmonary vessels, which rupture under the strain (9) (10). It has also been shown that there is another possible source for the bleeding, the presence of dilated veins in the bronchial tree (11). The prognostic significance of hæmoptysis varies with the cause. When the heart is not enlarged it is not serious. The bleeding itself is not dangerous, but it may point to advanced disease (12)

THE LEFT AURICLE. The left auricle may enlarge greatly, and then it extends to the right and becomes visible through the shadow of the large right auricle, or extends beyond it at a rather higher level. Cases have been recorded where the left auricle has reached the right side of the chest The aortic arch prevents expansion to the left; the mitral murmur, conducted into the huge left auricle, may be heard in the right anterior axillary line, (Plate 12) The left recurrent laryngeal nerve may be compressed and become paralysed, but the dilated pulmonary artery may be a factor here, as paralysis occurs with the large pulmonary artery of patent ductus arteriosus. Upward pressure may compress and splay the main bronchi, and even cause collapse of the left lung. The dilated left auricle may press on the spine and cause pain by erosion of the vertebræ (17). A dilated fibrillating left auricle may be the seat of a *ball thrombus* or myxoma. This may be attached or be free. Such a clot may suddenly occlude the mitral valve and cause syncope, or sudden death (13) The attack of syncope is marked by pallor, pains in the limbs, disappearance of the pulse (p 96).

Aortic Valvular Disease. Disease of the aortic valves alone of rheumatic origin is not uncommon. Out of 200 cases of rheumatic aortic valvular disease, the aortic valves were affected alone in 38 per cent; the *mitral* valve was also diseased in the remainder (14). In cases of mitral *stenosis*, *aortic* lesions were present in addition in about half (15).

The conclusion is that aortic disease occurs alone in ...

of the heart, usually on the left. They depend for their origin upon the interruption of the filling of the lungs with air by the movements of the heart. They are usually related to a particular phase of respiration, especially inspiration. They are sometimes very obviously an interrupted breath sound. Holding the breath, especially in expiration, abolishes them. Indefinite murmurs of this nature should always be investigated with the patient recumbent and standing. The site and extent of maximum intensity should be noted. Some are best heard between the apex and the sternum, and tend to spread towards the pulmonary area. There is one type, rather louder and coarser than the others, which is heard late in systole, following the first sound by an interval and running into the second sound. Its causation is obscure; it is not associated with any other abnormality and remains unchanged for years. It is no doubt harmless. The error it occasions is to mistake it for a presystolic murmur by taking the second sound for the first, and diagnosing mitral stenosis. Similarly, mitral stenosis may be erroneously diagnosed when an innocent apical systolic murmur is found in a nervous young adult with a loud mitral first sound and a third sound early in diastole. This is a common clinical combination, conspicuous when the patient lies on his left side.

It has been suggested that here the normal mitral opening is relatively too small for the rush of blood and so in a sense relatively stenosed; hence the signs (6). It seems more likely that the third sound is due to vibration set up in the wall of the empty ventricle by the inrush of blood early in diastole.

Cyanosis is apt to occur early in mitral disease. There appears to be an increase in the peripheral utilisation of oxygen, due to a slower flow of blood; cyanosis is then of peripheral origin. There is in some cases a decrease in the oxygen saturation of the arterial blood, the result, perhaps, of changes in the walls of the pulmonary alveoli. It has been suggested that there may be slight obstruction to the superior vena cava by some obstacle which the passage of a cardiac catheter reveals, possibly the large left auricle. This has been held to account for the cyanosis peculiar to the mitral facies (7).

Hæmoptysis is quite a common occurrence. *There are several* possible causes. There may be emboli causing infarction.

9 McGinn, White (1934) *Amer Heart J.*, 9 697
10 Stewart (1934). *Med Clin N Amer*, 18, 1917
(1944) *Amer Heart J*, 28, 445
163

eports, 83, 168

15 Stone, Feil
16 Ernstene, Schneider (1941) *Amer J med Sci*, 202, 737.
17. Ashworth, Morgan Jones (1946) *Brit Heart J*, 8, 207
18 Rosenthal, Feigin (1947) *Amer. Heart J*, 33, 346
19 Fertman, Wolff (1946) *Amer Heart J*, 31, 580
20 Hohngren (1946) *Acta Radiol*, 27, 171
21 Evans (1947) *Brit Heart J*, 9, 1

Calcification of the Aortic Valves. At autopsy it is not uncommon to find calcified aortic valves. Usually this is associated with much fibrosis of the valves and a severe degree of stenosis.

Pathology. The valves are thickened, fused and calcified. It may be difficult to decide whether the bicuspid condition of the valves was originally a congenital defect, or has arisen as a result of fusion from an inflammatory process. Fusion may also occur in the purely degenerative type.

Inflammatory Type In this sort rheumatic endocarditis has preceded the calcification. The main deposits of calcium salts are in the upper part of the valve and more on the outer surface (1, 2). The mitral valve is also diseased, and not uncommonly there is evidence of past pericarditis. There may be microscopical evidence of past myocarditis (3). There may have been a history of past rheumatism infection The sex incidence is about equal (1). It is held that the majority of bicuspid aortic valves in adults are the result of fusion through a rheumatic inflammation (4). Occasionally it seems possible that a healed subacute bacterial endocarditis has led to fusion and calcification (5)

Degenerative Type. In this the calcification is in the depths of the valve pocket and more on the aortic surface (1, 2). There are no stigmata suggesting rheumatism. The mitral valve is normal. There is a pure degenerative process of the collagen fibres which leads to calcification (6). In these cases females are far less common than males, and the subjects are older.

Clinical Features. Clinically the stenosis gives rise to the signs already described. Regurgitation occurs in about one half of the cases (7)

The presence of calcification can be demonstrated in skiagrams

one-seventh of all cases, and is about one-quarter as common as mitral stenosis.

AORTIC INCOMPETENCE is the usual finding. A blowing diastolic murmur is audible to the left of the sternum. It is generally most distinct at the third left intercostal space, but is often audible at each of the adjacent spaces on either side and also in the aortic area. The murmur is best heard in full expiration with the patient sitting up. The peripheral signs are not helpful in very early cases

AORTIC SCLEROSIS. Thickening and stiffening of the cusps leads to some narrowing of the outlet. Some grade of narrowing is not uncommonly associated with aortic reflux. Clinically aortic sclerosis is characterised by a loud, harsh systolic murmur, conducted up to the arteries in the neck. There is no thrill.

AORTIC STENOSIS. In addition to the loud, harsh murmur conducted upwards, there is always a systolic thrill over the aortic area. This is best felt with the palm of the hand, in full expiration, *the patient leaning forwards. The second sound is faint.* The pulse is anacrotic. The systolic pressure is often low and the pulse pressure small. As a result of rheumatic disease there is often a combination of aortic stenosis and incompetence, neither reaching the degree either may attain alone, and perhaps in consequence not ill-tolerated for a long time.

Associated with free aortic reflux angina pectoris may occur in the young. These attacks may take place at rest and during the night, as well as on exertion. There is usually a good deal of vasomotor instability. Nitrites relieve the pain. The attacks may be dangerous (16).

COMBINED AORTIC AND MITRAL DISEASE. *When the aortic* disease is accompanied by a mitral lesion, there appears to be less tendency for severe mitral stenosis to develop. This may in a sense be an advantage.

REFERENCES

1 ROTHSCHILD, KUGEL, GROSS (1934) *Amer Heart J*, 9, 586.
2 PARKINSON (1944) *Lancet*, 2, 657
3 BAILEY, HICKHAM (1944) *Amer Heart J*, 28, 578
4 MARKS (1936) *New Eng J Med*, 214, 411
5 BLOOMFIELD, LAWSON, COURNAND, BREED, RICHARDS (1946). *J. clin Invest*, 25, 639
6 BRAMWELL (1942). *Brit Heart J*, 5, 23
7 COSSIO, BERCONSKY (1939) *Amer Heart J*, 17, 1.
8 OPPENHEIMER, SCHWARTZ (1933) *Amer Heart J*, 9, 14

Tricuspid Disease. Some degree of rheumatic inflammation of the tricuspid valves is not uncommon. It may be present in about 20 per cent of cases with mitral stenosis (1). This agrees with another series where the figure was 22 per cent (2). As a result of this damage stenosis may develop. Stenosis of the tricuspid valve occurs in about 9 per cent (3) or 14 per cent (2) or 6 per cent (4) of autopsies on patients with rheumatic heart disease. Incompetence of the tricuspid valve may result from dilatation of the right ventricle apart from any valvular lesion. There may be slight thickening of the flaps and shortening of the chordæ tendineæ as a result of rheumatism, or it may be present in association with actual stenosis.

CLINICAL DIAGNOSIS. It has always been considered difficult to diagnose tricuspid disease, particularly *stenosis, with certainty*. An important sign is strong pulsation in the jugular veins when the patient reclines at forty-five degrees. Whereas this is, in fact, a sign of *tricuspid regurgitation* and so may be transient, as a result of relative incompetence. Cooke and White (5) hold that there is strong probability of tricuspid stenosis in a patient about forty or fifty who has had rheumatic heart disease, and who for years has exhibited strong systolic jugular pulsation with but little sign of congestive failure. Associated with the jugular pulsation goes expansile pulsation of the liver. This is best detected bimanually. In contrast to its size the liver is but little tender. The right auricle is usually greatly enlarged to the right, and shows clearly in the skiagram. The enlarged right auricle may push the œsophagus to the left, as may be seen in the antero-posterior position when it is filled with barium (6). (Plate 18.)

There is, as [illegible]
circulation (2 [illegible]
[illegible] ether,
[illegible]

The murmurs are *difficult* to distinguish. These cases have a severe mitral stenosis, and not uncommonly aortic stenosis and perhaps reflux as well (3). The mitral and aortic murmurs obscure those produced at the tricuspid valve. As auricular fibrillation is present in half to three-quarters of the patients, the tricuspid presystolic murmur will be absent. There may be pulmonary

if taken with sufficient penetration in a large number of cases, or seen on screening if the patient is thin. The shadow of the calcified valves moves up and down with the heart beat.

The disease usually appears in men late in life. The symptoms for a long time are often slight. There may be dyspnœa. About a quarter of them complain of angina pectoris (7). At this age there may, of course, be associated atheroma of the coronary arteries; but the severe aortic stenosis seems to be a cause of myocardial ischæmia. The narrow opening into the aorta and the rigid valves probably tend to reduce the coronary flow (8). It has also been suggested that the high intraventricular systolic pressure due to the aortic stenosis both increases the work of the muscle and occludes by compression the coronary arteries within it (9). Heart block has been noted resulting from the invasion of the bundle by the process of calcification.

Those patients are prone to syncopal attacks, particularly on exertion. These attacks appear to be due to deficient output, for the carotid sinus has not been found to be unduly sensitive (7). Ischæmic changes may be found in the myocardium without actual occlusion of the coronary arteries. The course of the disease in these cases of pure aortic stenosis is slow.

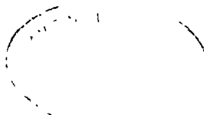
On the whole, it appears that when there is an associated mitral lesion, and the lesion is presumably rheumatic, death occurs at an earlier age than when the aortic lesion is uncomplicated and presumably degenerative and of later onset (10). Some pass on to congestive heart failure and go slowly downhill. Auricular fibrillation is unusual unless a mitral lesion is present as well as the aortic. *Quite a large proportion die unexpectedly* (11). *It is* not unusual to find calcified aortic stenosis in a man over sixty who has dropped dead without warning.

REFERENCES

1 ... *Heart J.*, 16, 43
2. ... *rt J.*, 17, 452
3 ... *Heart J.*, 15, 58
4
5 ... *h.*, 13, 389
6. ... 477
7 ... *led.*, 10, 1036
8 ... 76
9 ... 4
10 ... *Sci.*, 188, 1



PLATE 13
Tricuspid Stenosis. Mitral Stenosis.



reflux, and a presystolic murmur in the tricuspid area, similar to the Austin Flint murmur of the mitral area, has been described, which led to the diagnosis of a tricuspid stenosis that subsequently was not found (2).

The aspect of the patient may show a combination of cyanosis, pallor, and a slight tinge of jaundice (10). In spite of the jugular engorgement there may be but little œdema (8). Later in the course of the disease there is tendency for ascites to develop and recur after paracentesis. This often leads to œdema from pressure on the inferior vena cava.

The presence of the tricuspid stenosis seems to protect the pulmonary circulation from the engorgement that the accompanying mitral stenosis would cause. The two lesions tend to balance one another The diagnosis may be suspected when there is persistent jugular engorgement with hepatic systolic pulsation; and yet the expected degree of incapacity is wanting, and the patient may be fairly active, and free from pulmonary congestion. This is because the findings are not really those of congestive failure, but are due to mechanical obstruction at the tricuspid valve The patients may do better than might be expected and under proper management the course may be fairly prolonged—on the average of seven years from the onset of congestion (9). While the prognosis may be quite favourable in the older patient, in younger patients when there is active disease it is much more grave (2). In some respects they resemble cases of Pick's Syndrome.

There are several points in treatment. Venesection is obviously useless. Digitalis may be required to control the heart rate when there is fibrillation. Since the liability to ascites, and perhaps œdema, is the chief cause of disability, mercurial diuretics by mouth, or by injection, are likely to be needed, and may keep the the accumulation of fluid under control Paracentesis of the abdomen will be needed from time to time. The fluid intake must be carefully regulated, as well as the intake of sodium.

REFERENCES

1. STONE, FEIL (1933) *Amer Heart J*, 9, 53
2. [illegible] (1941) *Brit Heart J*, 3, 147
3. [illegible] *J*, 23, 739
4. [illegible] 101.
5. [illegible] *Amer Phys*, 54, 199
6. [illegible] *Soc Med. Hop*, Paris, 52, 594
7. [illegible] *Path*, 30, 7

Altschule, Blumgart (1937) *Amer. Heart J.*, 13, 589
Thompson, Levine (1937) *Amer. J. med. Sci.*, 193, 4
Aceves, Carral (1947) *Amer. Heart J.*, 34, 114

Adherent Pericardium. Pericardial adhesions are nearly always a sign of previous heavy infection of the heart. If the adhesions are confined to the sac they do no harm, and obliteration of the sac does not increase the work of the heart. Extra-pericardial adhesions may cause hypertrophy. The only reliable sign of adherent pericardium is systolic retraction of the chest wall. Retraction must be distinguished from recession. Where the hypertrophied right ventricle thrusts forward there may be recession outside the cardiac area to the left. Broadbent's sign is systolic retraction of the eleventh and twelfth ribs due to dragging by adhesions between the back of the left ventricle and the diaphragm. Extra-pericardial adhesions may be seen on screening. Fixation of the heart may be seen when the patient leans from side to side; but large hearts do not move much. Probably most, if not all, of the hypertrophy once ascribed to adhesions in the pericardial sac are due to associated valvular lesions. It is noteworthy that some years after acute pericarditis, particularly in young adults, the heart may show no abnormality. Pick's syndrome does not result from rheumatic pericarditis.

Prognosis

The later prognosis of chronic rheumatic heart disease depends on the severity of the infection. With a severe attack the child may die soon. The prognosis may be quite good in a mild attack; the young adult has a better chance of slight cardiac damage. Another factor is the persistent recurrence of latent damage, causing finally severe valvular lesions. Between the ages of five and thirteen years the recurrence rate was 25 per cent; from fourteen to sixteen it was 8 per cent, and from seventeen to twenty-five 2 per cent (1).

In a series of war pensioners, watched for ten years, it was noted that of the cases with mitral stenosis, 24 per cent were no worse and 30 per cent had developed auricular fibrillation. Of those with aortic reflux 34 per cent were unchanged, and of those with combined lesions the figure was about the same (1). In a small group with aortic stenosis 60 per cent died within the ten years (2). In a series of necropsies, excluding cases under twenty

So far the evidence is inconclusive. No doubt the incidence of cardiac lesions in these cases may be high. But in these old patients many of them may not be of rheumatic origin. These diseases affect the same tissues of the body and so may provoke rather similar responses. But until more is known about the nature of their causes it will be difficult to decide whether they are the same. On the whole the balance of the clinical and pathological evidence is against their identity. No doubt some susceptible patients may suffer from both at different ages. There is enough evidence, however, to stimulate further interest in the nature and incidence of such cardiac defects as do occur in rheumatoid arthritis. More clinical observations would be welcome. That rheumatoid arthritis causes endocarditis is very doubtful

REFERENCES

, 42

t J, 28, 1

d, 21, 551

Int Med, 67, 241

Path, 30, 70

Lupus Erythematosus Disseminatus

(*Libman-Sacks Disease*)

The association of a form of endocarditis with lupus erythematosus was first pointed out by Libman and Sacks in 1924 (1). The cutaneous lesion with its peculiar distribution across [illegible] There [illegible] is that [illegible] cases in the United States show that this disease of the skin may be associated not only with a peculiar form of endocarditis, but also with lesions in many of the organs of the body and a profound constitutional disturbance, which seems to be fatal in nearly all cases.

The cause is quite unknown, but there are two curious points in the incidence. It is almost entirely confined to women between the ages of fifteen and forty-five, coinciding with the years of menstruation.

The onset may be gradual or acute. There is fever, prostration and rapid wasting.

years, the highest incidence was between the ages of forty and fifty, but 10 per cent reached sixty years (3).

REFERENCES

1. GRANT (1931). *Heart*, 16, 275.
2. WILSON, LUBSCHEZ (1944) *J Amer med Assoc.*, 126, 477.
3. DAVID, WEISS (1932) *Amer. Heart J.*, 8, 182.

The Heart in Rheumatoid Arthritis. Rheumatic fever and rheumatoid arthritis have certain things in common. In particular there is the arthritis. But the distribution of the lesions, the course of the changes in them and the final results are different. They may both have nodules. They respond, however, differently to salicylates.

The question which has received some attention is whether they are really manifestations of the same disease, and whether there are any cardiac lesions in rheumatoid arthritis which resemble those of acute rheumatism. In twenty-three cases studied at autopsy, six had endocardial and myocardial lesions which were somewhat similar to those resulting from rheumatism. In two there were pericardial adhesions. All the patients were old, and none of the lesions was active or recent (1). In four of these the clinical diagnosis of heart disease was made. In another series of thirty-eight cases, the autopsies showed cardiac lesions in thirty-three. In twenty-five of these the lesions were thought to have been rheumatic in origin It is curious that in some the results of pericarditis were found alone without valvular disease; in ten others the two were present together. The myocardial lesions were unreliable, for such complicating factors as coronary disease and hypertension were not uncommon at the ages at which these patients died (2). *Clinically the history of rheumatic fever* was rarely given but that does not exclude rheumatism. In about half the cases the clinical diagnosis of heart disease was not made, although for the most part they had been long in hospital.

The histological conclusions as to the identity of the nodules are not in agreement. Some authors think that they are the same (3, 4), and others think that they are different (5, 6). Clinically the rheumatoid nodules are often larger and last very much longer. Differences might be due to the age of the nodule.

A further series of thirty-three cases showed only one with a cardiac lesion of dubious origin (7).

very difficult. It is a widespread disease with very variable clinical appearances. The diagnosis is not likely to be made until it is apparent that an unusual assortment of lesions are present together (8). The prognosis is usually very bad, but recovery after penicillin has been reported (9). There is resemblance to acute rheumatism in the cardiac lesions and the arthritis and anæmia. The renal lesions and splenic enlargement may suggest infective endocarditis But the blood culture is never positive; there are no emboli nor clubbing of the fingers. Pleurisy is rare in rheumatism and subacute bacterial endocarditis, nor does glandular enlargement occur as a rule, except in the rheumatoid variety. It would appear that in this country the disease is very rare, or is not diagnosed, for there is but little reference to it (6).

REFERENCES

1 Libman Sacks (1924) *Arch int Med*, 33, 701
2 Gross (1940) *Amer J Path*, 16, 375

mer. Phys, 50, 139

Subacute Infective Endocarditis

Aetiology. The streptococcus viridans is nearly always the infecting organism In a case that runs an atypical course, or is resistant to treatment, special methods of culture may show that more than one organism is present. There may be more than one variety of streptococcus, or an associated infection with gonococci (1) In the ordinary case the organisms enter the blood stream from some focus of infection. It is not uncommon for an apical infection at the root of a tooth to cause a transient bacteremia, particularly on dental extraction. The organisms attack previously damaged valves or congenital deformities.

Previous Valvulitis. It is rare for the aortic valves, when previously damaged by syphilis, to be attacked. Those which are prone to secondary infection are those damaged by rheumatic disease There are two theories as to the mode of attack. One supposes that the organisms reach the inside of the valves by their blood vessels. These are more numerous after some preceding

Cardiac Lesions. Endocarditis. This is verrucose in type; the warty vegetations are profuse, yellow, and reaching the size of a grape or apple pip. They appear in ridges, or massive thrombotic clusters, or in flat spreading sheets. They are found on both surfaces of the valve flap, spreading down the chordæ tendineæ, *and in the pockets between their attachments under the valve.* The mitral valve is most often attacked, and the others in about equal proportions The valvulitis does not spread from the root of the valve as in rheumatism, but is more superficial Scarring is less (2). The mural spread of the vegetations into the auricle is notable. There is no tendency to embolism. Actual ulceration or destruction of the valve does not occur. There may be a secondary bacterial invasion.

Myocarditis. Here the lesions are principally degenerative. The chief injury is to the connective tissue cells. The damage affects the collagen fibres, and there is degeneration of the fibroblasts *There may be a certain amount of fibrosis; nothing* resembling the Aschoff's body of rheumatism is ever seen.

Pericarditis. This is more superficial and less intense than that of rheumatism In the early stages it is fibrinous Adhesions may become extensive later, but they are not dense. The incidence of this lesion may be high (7).

There may be extensive *pleurisy,* but usually the lungs themselves escape (3) *Pneumonia,* however, has been noted (4)

Renal Lesions. The lesions are glomerular. These become hyalinised in a patchy way, so that the degenerate areas look like "wire loops" (3). The urine shows albumen red corpuscles and casts. *The lesions in the kidney may be so extensive that the* blood pressure rises and there may be papilledema and renal failure (4) (5). The spleen and liver may become enlarged. There may be arthritis. *Glandular enlargement may be general.*

The characteristic skin lesions may not develop until the disease has been present some time. Typical examples of this sort of endocarditis have been found in patients who have never had any erythematous lesions (2). In addition there may be purpura. The blood shows anæmia and leucopenia and thrombocytopenia. Blood cultures are negative

The course of the disease may be anything from eighteen months to five years. The diagnosis, in the absence of the rash, may be

fever. The general health prior to the onset of the symptoms of the bacterial infection was noted as excellent in about 78 per cent, and good or fair in the remainder. The great majority of patients have suffered no inconvenience from their hearts since their attack of rheumatic fever (7). Infective endocarditis is unlikely to arise in patients with chronic heart failure, and it rarely occurs in a heart that has auricular fibrillation (8). Auricular fibrillation is likewise a very rare complication of infective endocarditis.

MORBID ANATOMY. *Valvular.* Large soft vegetations are formed, which are often greenish in colour. The infection spreads widely over the adjacent surfaces of the valve from the point of origin. From the aortic cusps the infection may reach the ventricular wall. The intima of the aorta may be invaded and a mycotic or bacterial aneurysm may form as the wall is penetrated (9) In this case there was no fever. Sometimes the intima of the aorta is infected primarily, particularly on an atheromatous or syphilitic patch. A mycotic aneurysm of the pulmonary artery has ruptured; the infection was associated with a patent ductus arteriosus (10). From the mitral valve the vegetations spread down the chordæ tendineæ and up into the auricle. The organisms are on the surface of the vegetation and also deep in the valve at the edge of the advancing infection The destruction of the valve is relatively slight compared with the luxuriance of the vegetations.

Myocardial. These lesions (Bracht-Wæchter bodies) are present in 95 per cent of cases. They are the result of various emboli of different sizes. Infarcts are actually very rare; the vessels on which the emboli lodge are so small and the anastomoses are too good (11). But the result is that there are very numerous minute myocardial lesions of embolic origin, which no doubt impair the efficiency of the myocardium in the long run (12).

Pericarditis is very rare

ONSET. The onset is usually insidious, with the symptoms of vague ill-health, lassitude, slight fever, sweating, indefinite rheumatic pains about the body, and some loss of weight. Occasionally the illness starts quite definitely with what may appear to be an influenzal attack Embolism may sometimes provoke a more dramatic onset.

Clinical Appearance. When well developed, the signs are

valvulitis. The damage in the capillaries just under the endothelium leads to the deposit of platelets and fibrin upon it. There then results a nidus for the further growth of bacteria (2). The other theory is that the streptococci attack the surface of the valves directly. Roughened areas in the endothelium, and the presence of minute thrombi or platelets give them a starting place (3).

There is some evidence that the rheumatic valvulitis in some cases is still active (4), and consequently the valves are vascular, with damaged endothelium suitable for re-infection.

In a series of children dying of infective endocarditis, Aschoff bodies were present in the hearts of all (5). It is probable that the very hard, scarred valves of late mitral stenosis are not often infected. Clinically it has been pointed out that those producing a loud systolic murmur are most vulnerable (3).

Acute Infective Endocarditis. Virulent organisms, such as pneumococci, pyogenic streptococci, staphylococci and gonococci, may attack healthy valves.

This type is relatively uncommon. The disease may attack the young and healthy, or the aged and feeble. Males are affected more than females. The incidence on aortic and mitral valves is about equal. The illness starts suddenly with high fever, rigors, sweating. The symptoms are those of a septicæmia. Murmurs, when they appear, show the localisation of the disease. Embolism occurs in the usual sites. There is soon great prostration, severe anæmia and rapid wasting. The disease runs a short fatal course of a few weeks, unless treated with full doses of penicillin.

Congenital Defects. Those most prone are such as involve the passage of blood through a small channel, such as the patent ductus arteriosus, patent interventricular septum; and aortic stenosis and pulmonary stenosis. The infection tends to occur in the second and third decades. In a series over two years of age of infected congenital defects, 42 per cent had patent interventricular septum, 28 per cent a patent ductus, 29 per cent uncomplicated pulmonary stenosis, 28 per cent Fallot's tetrad, and 21 per cent congenital bicuspid aortic valves (6).

Incidence. Men are infected more often than women. The proportion is about 3 to 2 under the age of thirty, and 3 to 1 over that age. About one-third of patients gave a history of rheumatic

sion and perhaps peritonitis from gangrene of the gut. A bacterial aneurysm (mycotic) may form in a peripheral artery where the embolus lodges; the internal arteries or those of the limbs may be affected, The aneurysm may rupture. They may be multiple (13). Bacteria have been demonstrated in the wall of the vessel affected (14)

Cutaneous Embolism. Petechiæ. Oval petechial hæmorrhages appear in the skin and conjunctivæ. Sometimes the larger ones have white centres. They often appear in crops.

Osler's Nodes. These are small painful pink areas on the palmar surfaces of the fingers and palms and on the corresponding areas of the feet. They are small areas of inflammation on the true skin, in the centre of which is an arteriole. They fade after a few days, and never suppurate. They tend to appear quite early in the disease and may be the first indication. They are important because they are absolutely diagnostic. Splinter hæmorrhages may occur under the nails.

Arthralgia. Sudden pains occur in the joints without any effusion. Sometimes the skin near the joint becomes reddened. These disturbances are quite transient.

Diagnosis. It is only in early cases that this presents difficulty. The possibility should be borne in mind in any case of mild rheumatic heart disease who complains of general ill-health, with intermittent fever.

Blood Culture. This should be done repeatedly if need be. By modern methods positive results are obtained in a large proportion of cases But there may be a bacteria-free phase which lasts some time.

In the aged the disease is *more difficult* to recognise. As is so often the case, old age considerably modifies the picture, and the diagnosis may be missed The constitutional symptoms are severe and progress rapid, prostration is considerable; these may be classified as acute cases (15). The subacute variety is also often missed The picture is *frequently* obscured by the multiple pathological states so often present together in the [illegible] d. It is [illegible]

[illegible] months [illegible] years. Embolism often caused death. Apart from this the patient steadily went downhill, with increasing emaciation and anæmia, and a terminal heart failure.

characteristic. There is persistent fever, ranging from 100°F. to 102°F. Rigors are rare; sweating is often profuse. A curious earthy pallor—*the café au lait complexion—is almost diagnostic.* There is progressive loss of flesh.

Cardiac Signs. These may be confusing, as there is usually evidence of an antecedent valvular lesion; the common finding is a systolic murmur at the apex, or a aortic diastolic murmur at the base. If there has been no previous valvular disease the mitral murmur may be quite inconspicuous for some time. The aortic diastolic murmur is more readily detected early.

Clubbed Fingers. This is an important sign, for it can be detected early, probably after three weeks. The change is not gross and first appears as a filling in of the sulcus at the root of the nail, best seen when viewed from the side. The pulp becomes a little full and bulbous. There is nothing comparable to the gross clubbing of pulmonary disease, or of congenital lesions of the heart. The fingers are pale and the tips are pink.

Spleen. There is appreciable splenic enlargement in nearly all cases. The increase in size is not great, but the spleen is moderately firm. The enlargement is due to toxæmia, with the added effect *of infarction in many cases.*

Anæmia. There is a secondary, or hypochromic, anæmia, which tends to increase as the disease advances There may be but little leucocytosis, but there is usually some relative increase in the number of the polymorphs. The sedimentation rate of the red cells is increased.

Embolism. This is common and the results vary a great deal, depending on the size of the emboli.

Splenic Infarction, with sudden local pain and perhaps friction sounds is almost constant.

Renal Infarction may cause sudden severe pain in the loin. *At autopsy the numerous minute* sub-capsular hæmorrhages have given the name of "flea-bitten kidney." Red cells are commonly found in the urine in small numbers, apart from occasional frank hæmaturia, resulting from damage to the glomeruli by minute emboli.

Emboli may reach the cerebral arteries, commonly the middle cerebral, causing hemiplegia; the retinal arteries, disturbing vision; and the mesenteric arteries causing acute abdominal pain, disten-

REFERENCES

1 ORGAIN, POSTON (1942) *Amer Heart J*, 23, 823.
(1943) *Amer Heart J.*, 25, 478
Med, 55, 173
204, 324
3, 60.
, 692
64, 336
115
17
211, 395
18 *clin Invest*, 24, 231.
19
20
21

Cardiovascular Syphilis

INCIDENCE. Deaths from cardiovascular syphilis accounted for about 3 per cent of autopsies in this country (1). About the same figure has more recently been found in the United States (2). The prevalence of the cardiovascular lesions is shown by an incidence of 80 per cent in autopsies on syphilitic patients (3); and 70 per cent of patients with general paralysis of the insane showed them (4) Clinically 3 per cent of patients attending a syphilitic clinic had aortic incompetence, presumably of syphilitic origin (5).

Aetiology. During the septicæmic stage of secondary syphilis all organs are probably invaded by spirochætes. The lungs probably receive large numbers, which are filtered by the lymphatics into the mediastinal glands. From this area they probably spread by the lymphatics to the first part of the ascending aorta. The latent period between infection and the development of these tertiary lesions is from fifteen to twenty years: very often there is no recollection of the primary infection (6).

MORBID ANATOMY *Aortitis.* The initial lesion is often found just above the attachments of the aortic valves. It is frequently triangular in shape and situated just about the commissures. The patch is due to thickening of the intima and is pearly grey in appearance and raised above the surface. The process spreads

TREATMENT. The introduction of large doses of penicillin has now completely changed the outlook for many patients from certain death to good prospects of recovery. The principle is that the treatment must be protracted and intensive: inadequate treatment to start with may prejudice success later. The dose should be 0.5 mega units (500,000 units) daily for twenty-eight days, but five or six times this dose may be needed. For this 60,000 units are given intramuscularly every three hours. The volume can now be quite small and a fine needle used. Instead of the watery solution an oily one, containing 200,000 units, may be given at eight hour intervals. Three or four such doses of the watery solution a day may be effective. It is too early yet to judge the efficiency of treatment with penicillin. It seems probable that perhaps 75 per cent are controlled, at any rate to start with (17). In one series of 17 cases, 14 had recovered fully after eight to twenty months. Here the daily dose was anything from 0.3 to 3 mega units (17). In another series 8 were cured after six months out of eleven, on rather smaller doses (18). In a further series two-thirds were reported cured after one to three years (21).

A longer interval of follow-up is needed to say how long they remain well. The early diagnosis no doubt increases the chance of success. The resistance of the infecting organism to penicillin does not seem to be important within wide limits. Relapse is likely to occur within a few days of inadequate treatment; but after a month's freedom following a full course relapse seems to be rare (17). Should a relapse occur the second course should last two months. It is doubtful whether heparin is of any use as adjuvant to treatment; in fact, it may be dangerous (20).

In spite of the healing of the infection in the damaged aortic valves, failure of the left ventricle may come on. Possibly the healing process increases the incompetence. On the other hand we have seen it lead to aortic stenosis. Healed infections have been found at autopsy, but, in the depths of one, cocci were visible (19).

PROPHYLAXIS. It will be well worth while to give penicillin for a day or two before and after any minor operation, such as dental extraction or tonsillectomy, to any patient with a valvular lesion of the heart.



PLATE 14

General dilatation of aorta from Syphilitic aortitis. Calcification of posterior part of arch. Dilatation of left ventricle from aortic reflux.

To face p. 76

round the vessel and distally as far as the origin of the great vessels from the arch. There may be multiple areas of this character. In addition to the intimal proliferation there is usually irregular puckered scarring to be seen. When stretched, the aortic wall is found to have lost its elasticity. It may be obviously thinner than normal or actually pouched in places. Histologically, the vasa vasorum undergo obliterative endarteritis. The perivascular spaces are full of lymphocytes; the elastic fibres of the media degenerate and disappear, being replaced by fibrous tissue and lymphocytes. The intima is thickened and usually hyaline. The aortic wall is thus weakened and tends to stretch, so that aneurysms may form. Spirochætes are seldom seen.

Valvulitis. From the commissures the thickening spreads along the free margins of the cusps of the aortic valves. The whole cusp later may become thickened and retracted and everted down towards the ventricle.

Aortic Incompetence results from this retraction and eversion. The swelling at the commissure tends to push the cusps apart and so helps to cause regurgitation. Stretching of the aortic ring may render the valves incompetent even when they are healthy (7). Aortic stenosis never results from syphilis alone. The mitral valve and the valves on the right side are not affected.

Stenosis of Coronary Ostia. If the intimal proliferation occurs near the mouth of the coronary artery as it leaves the aorta, the lumen will be narrowed. If the coronary artery arises from the sinus of Valsalva it may escape, for the syphilitic proliferation of the intima begins above the level of the cusps. But it may spread downwards. If the coronary artery arises higher up its mouth is more likely to be obliterated.

The coronary ostia are obstructed in from 30 to 70 per cent of cases (8). The right coronary artery is more often occluded than the left.

Aneurysm. The aortic wall, weakened by syphilis, stretches under the shock of systolic filling. The ascending portion becomes dilated and may show irregular pouching. Aortic reflux may relieve the strain, and aneurysms are less likely to form if reflux has developed early. Aneurysms occur in about 38 per cent of cases of cardiovascular syphilis (8). (Plates 14 and 15.)

Myocardial Lesions. These are rare. The occlusion of the ostia



PLATE 14

General dilatation of aorta from Syphilitic aortitis. Calcification of posterior part of arch Dilatation of left ventricle from aortic reflux

To face p. 78



PLATE 15

Aortic Aneurysm (posterior).

of the coronary arteries hardly ever leads to infarction of the myocardium. When this does occur it is the result of atheromatous degeneration along their course. Sometimes a fibrous zone spreads down into the top of the septum from the aorta and may involve the bundle of His. Microscopically there may be patchy areas of ischæmic necrosis and fibrosis (9)

Clinical Features. SYMPTOMS. The aortic reflux will sooner or later cause embarrassment of the left ventricle and lead to dyspnœa on exertion. But the asymptomatic phase may be surprisingly long, perhaps two or three years, the patient doing active work the while (5). In the later stages paroxysms of dyspnœa at night are common.

Pain. This is substernal in character, of the cardiac type, occurring on exertion. It is due to ischæmia of the myocardium and associated with the occlusion of the coronary ostia.

The combination of an enlarged, overworked left ventricle, whose blood supply is curtailed by ostial obliteration and hampered by a low diastolic pressure, makes its development easy. An interesting type of pain occurs at rest, and seems to be associated with recumbency, particularly at night.

The pain is often prolonged and may be relieved by nitrites, or pressure on the carotid sinus. Sometimes attacks of dyspnœa accompany the pain (paradyspnœic angina). The horizontal position introduces several adverse factors. The cardiac output rises (10). The lungs are probably more engorged, and the elevation of the diaphragm may cause embarrassment. Possibly reflex factors also play a part The underlying cause is certainly generalised cardiac ischæmia (11) Pain probably does not arise from a syphilitic aorta until there is sufficient aneurysmal dilatation to cause pressure on surrounding structures.

AORTIC INCOMPETENCE This may be due to retraction of the valves, or dilatation of the ring, or both together. The sign is the typical diastolic murmur, heard over the base of the heart. Usually it is loudest in the aortic area, but it may appear to the left of the sternum It may be curiously loud and musical; one cusp is then found to be everted (6). The regurgitation tends to be free and progressive The peripheral signs are conspicuous; pulsating arteries, Corrigan pulse, and Duroziez's murmur are easily demonstrated. The aortic reflux leads to dilatation and hypertrophy of

the left ventricle, marked by a sustained heaving apex beat. If there is much dilatation the enlargement may be gross. There may be less hypertrophy if the coronary ostia are stenosed.

Austin Flint Murmur. Associated with the murmur of aortic reflux, a soft low-pitched presystolic murmur may be heard at the apex. It is never associated with a thrill and is less rough than that of organic mitral stenosis. It was originally suggested that this murmur was due to vibrations set up by the entry of blood into the ventricle at auricular systole through a mitral orifice [illegible] the aorta. It has been pointed out that [illegible] mitral cusp may be found at [illegible] eam has impinged. In these cases the right anterior aortic [illegible] as most affected (12).

AORTITIS The early diagnosis is difficult. There may be a low-pitched aortic systolic murmur. The aortic second sound may become loud and hollow sounding: this is significant if the blood pressure is normal Changes in the size and contour of the first part of the aorta may be detected on radiosopy. The ascending part of the aorta is dilated and its shadow extends out to the right further than that of the right auricle. The edge is often hazy and the contour may be irregular. The "knob" may be prominent, and wider than normal when measured vertically. The pulsation may be increased; but allowance must be made for the effect on the pulsation of any aortic reflux that may be present. When the aorta is viewed in the left anterior oblique position the width of the arch can be measured; an increase in diameter over 6 cms. is likely to be due to syphilis. In the right anterior position the border may show bulging, and the shadow no longer taper upwards. There is also enlargement of the aorta in hypertension. Here there is more elongation or "unfolding" and the borders are more or less parallel The "knob" is prominent and higher than normal, but not necessarily much wider. In older patients with atheroma the aorta enlarges. Calcification can often be made out It must be remembered that atheroma and syphilis are often found together. The early diagnosis is therefore far from easy.

Aneurysm. The signs of aneurysm are well known The disease is less common nowadays than in years gone by. The diagnosis on radioscopy of a thoracic tumour is obvious enough. The classical

difficulty in differentiating an aneurysm from a thoracic growth is often present, for tumours may show transmitted pulsation. A vascular pulsating secondary deposit from a hypernephroma may closely simulate aneurysm. The pulsation may be softer and slower to expand than a normal aortic thrust (13) (See Plates 14 and 15). Angio cardiography will help in diagnosis in these cases, but the technique is difficult.

The aneurysm may press on the pulmonary artery and cause stenosis The right ventricle will then enlarge and fail, and cyanosis may be severe (14) The pulmonary valve may become incompetent. The diagnosis from aneurysm of the pulmonary artery itself is difficult (15). Here the trunk is usually affected and the valves are incompetent. The right ventricle enlarges and fatal failure soon supervenes (16)

When an aneurysm ruptures into the pulmonary artery a syndrome may be recognised The patient becomes intensely breathless A continuous murmur and thrill are detectable in the pulmonary area. The right ventricle enlarges and fails. Both the aorta and pulmonary artery are enlarged. The patient may survive several months (17). Rupture into the right auricle may be recognised by sudden precordial tightness, and a continuous waxing and waning murmur. The murmur is conducted down into the engorged, tender, pulsating liver, and down the inferior vena cava. The right auricle becomes engorged; atrial trachycardia and fibrillation are common. The signs in the peripheral arterial system are those of aortic incompetence (23).

Congenital syphilis causes cardiovascular lesions only very rarely.

Bacterial Infection. Syphilitic valves are far less often attacked than those damaged by rheumatic endocarditis. At post mortem the underlying syphilitic lesion may be overlooked unless careful attention is paid to the commissures (18). Small vegetations may be found on the bases of the cusps and on their ventricular surfaces The mitral valve may be affected as well, following the aortic lesion (19)

Rheumatic Infection The association of syphilis and rheumatism is uncommon. There may be an aneurysm with mitral stenosis, or a case with mitral stenosis may develop aortic reflux, and the Wassermann reaction may be found to be positive.

It may be possible to detect the commissural lesion of syphilis

and the valvulitis of rheumatism together, and find Aschoff's nodes in the myocardium. The coronary ostia may be involved (20).

The presence of the syphilitic lesion seems to shorten the usual course of the rheumatic lesion (21). It has been suggested that rheumatism is really the underlying defect which predisposes to bacterial infection, and that it is actually present when apparently syphilitic valves are attacked (22).

DIAGNOSIS. The diagnosis of cardiovascular syphilis is not difficult when it is remembered that it is a disease primarily of middle-aged men. Men are attacked six times as often as women. Various series show that the Wassermann reaction is positive in about 85 per cent of cases. The positive reaction may not necessarily *refer to the heart and aorta. Signs of the disease may be* present elsewhere in the body: there will still be a few patients in whom the diagnosis cannot be made with certainty. In this respect the words of Vigo (1785) may be quoted: "When you meet with a disease that does not respond to the ordinary remedies, *you may think that this is the disease called French.*"

COURSE AND PROGNOSIS. The combination of left ventricular overload from aortic reflux, and myocardial ischæmia from obliteration of the coronary ostia, causes in most cases steady and progressive failure of the left ventricle. An alternative may be the rupture, or pressure of an aortic aneurysm. Once failure has begun in these cases, its course is but little amenable to treatment as a rule. When pain indicates ostial obliteration sudden death is common. The sudden death is no doubt due to the poor blood supply to the myocardium resulting from the low diastolic pressure and coronary obliteration (2). The prognosis is bad as a rule once symptoms have developed. The average length of life, once symptoms have developed, is probably from two to three years, but adequate treatment may prolong this. Much depends on the patient's occupation. Those who have had laborious work do badly.

Treatment. The pathology of the disease makes treatment rather unsatisfactory. The course should start with bismuth and potassium iodide. Arsenic should not be given at first, and then only in small doses to begin with in order to avoid a Herxheimer reaction. Particular caution is needed with arsenic if there has been pain or dyspnœa. If there is heart failure, this should be treated before starting on the anti-syphilitic course.

A programme of anti-syphilitic treatment might be as follows. If there is heart failure, that must be dealt with first. If there is much cardiac pain on exertion the patient should be confined to bed for two or three weeks. If the lesion has been found because of mild symptoms only, or by chance, the patient may be up and about while under treatment.

Bismuth. This may be given, in doses of 1 to 2 grains in an oily suspension, by intramuscular injection every 4 to 7 days for a month, and then in 3-grain doses for another 4 to 8 weeks. The B P. injection of bismuth (8 to 15 minims) contains 20 per cent of precipitated bismuth (1½ to 3 grains) 4 cc. of quinine iodobismuthate may be given thrice weekly.

Potassium Iodide. At the same time 30 to 45 grains should be given daily.

Mercury This has been largely superseded by bismuth. Injections of the mercurial cream (B.P. injectio Hydrargyri) may be given in 5 or 10 minim doses; or the pill of mercury and chalk may be taken by mouth 1 grain daily.

Arsenic After 8 to 12 weeks of this treatment arsenic may be started. Neoarsphenamine may be given intravenously *in small* doses to start with, 0.10 to 0.20 gramme at weekly intervals, through, six or eight injections to a maximum of *0.45 gramme*.

Some prefer to give Stovarsol (sodium acetyl arsenilate) by mouth, starting with 1 gr. twice daily for four days, and then thrice daily for two days; the course is then repeated after an interval of three days and continued for two or three months. Later intramuscular arsenic is given Some authorities give no arsenic to patients over the age of fifty years (24).

The role of *penicillin* remains to be ascertained There are reports of severe Herxheimer reactions, but we have noted encouraging improvement in some cases. It should not be given to start with, but after iodide and bismuth.

REFERENCES

1 Coombs (1932) *Quart J Med* 1 179
2 [illegible] 24 740
[illegible] 25, 115
[illegible] *Sci*, 203, 202.
[illegible] Kilgore? — [illegible]LAND (1930) *Amer Heart J*, 6, 1.

9 LOVE, [illegible] 18, 154
10 McMic
11 EVAN
12 GOULE
13. LEWIS (1940). *Brit. Heart J*, 2, 260
14 GARVIN, SIEGEL (1939) *Amer. J med. Sci.*, 198, 679
15 DICKENS (1940) *Brit Heart J.*, 2, 247
16 BOYD, McGAVACK (1939). *Amer Heart J*, 18, 352.
17 PORTER (1942) *Amer Heart J*, 23, 468
18 BRAUNSTEIN, TOWNSEND (1940) *Arch int Med*, 66, 441
19 BRAUNSTEIN TOWNSEND (1940) *ibid*, 65, 957
20 LISA *et al* (1942) *Arch Path*, 33, 37
21 SWANSON (1939) *Amer Heart J*, 18, 572
22 KOLETSKY (1942) *Amer Heart J*, 23, 208
23 LEARY (1940) *New Eng J Med*, 223, 789
24 McELLIGOTT (1946) *Brit J ven Dis*, 22, 171
25 HERRMANN, SCHOFIELD (1947) *Amer Heart J*, 34, 87

Diseases of the Pericardial Sac

Congenital Defects. These are very rare. They usually consist of a deficiency of the sac on the left side. The hole may be one through which the heart may herniate and become strangled. Sometimes the left pleural cavity and the pericardial sac form one cavity. Pleuro-pericardial infection seems to have a high incidence in these cases (1). Cysts are occasionally met with.

Infections

Infections of the pericardial sac may lead to acute and chronic inflammatory changes. The nature of these depends upon the cause. The work of the heart may be affected seriously, so that it is unable to fill in diastole; this effect is produced in two rather different ways. A large effusion, which may be serous, purulent, or hæmorrhagic, or indeed a pure hæmopericardium, can cause tamponade. A chronic pericarditis may produce a shrunken and constricted sac.

Fibrinous or Dry Pericarditis. This is not uncommon It frequently appears in a rheumatic pancarditis. It is found over an infarct of the myocardium; it appears in the last phases of chronic nephritis. In some cases the cause and association are quite obscure. The dry rub, often first heard at the base, is the diagnostic sign. It has always been customary to note that the rub varies with the pressure of the stethoscope. Analysis with sound records shows that moderate pressure with the end-piece increases the intensity of the vibrations transmitted through the chest wall. As the pressure increases these are damped, and finally

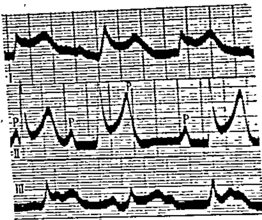


FIG 17A
Acute pericarditis Complete heart block

disappear. These auscultatory variations may be due to alterations in the frequency of the sounds transmitted, and to the damping effect of pressure. The "to and fro" character of the sounds, when recorded simultaneously with the electrocardiogram, is due perhaps to friction at auricular and ventricular systole (2)

The combination of pain, which may be very severe and referred to the base of the neck or left shoulder, fever, friction sounds, may simulate myocardial infarction; but the onset is less sudden, the symptoms less severe, the fever higher, and shock is absent. The changes in the electrocardiogram may need to be carefully distinguished from those of infarction (3) (see p. 205) (Figs. 17A and 17B) When the pericarditis is of rheumatic origin, the onset is more gradual than that of indeterminate origin. With this type in young adults there is no arthritis or leucocytosis (53).

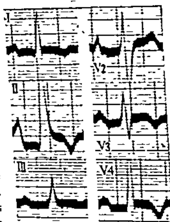


FIG 17B
The same three days later Note bowed inversion of T in leads 1, 2, V_2 and V_4 Q-waves are absent

PERICARDIAL EFFUSION—AETIOLOGY. Tuberculous pericarditis is an entity that needs special consideration. Pyopericardium may arise by direct spread from an empyema. when it is usually pneumococcal. It may be streptococcal, as part of a septicæmia; or a staphylococcal infection with pyæmia, may cause a very large

effusion. Rheumatism causes a serous effusion at times. Some serous effusions are obscure in origin. A form of pericarditis with effusion has been described following quite trivial infections of the upper respiratory track. They run a benign course, but there is the possibility of adhesions later (4). Myxœdema has been recorded, and it is suggested that the enlargement of the myxœdematous heart is chiefly due to pericardial effusion (Plate 16). Hæmorrhagic effusion may be tuberculous or neoplastic. Hæmopericardium may result from trauma, or escape of blood from a ruptured aorta or ventricle. Most of these cases die very quickly. (Plates 17A and 17B.)

DIAGNOSIS. The diagnosis is easily missed. The increase in the cardiac dullness to the right (in Rotch's angle) and upwards to the left and beyond the apex beat is important; and perhaps the disappearance of previously observed friction sounds. The heart sounds become muffled and the apex beat obscured. The skiagram shows a pear-shaped shadow, which is fairly typical, although a greatly dilated heart sometimes assumes this appearance. Other points are the small range of cardiac pulsation, the flattened aortic knob, and the diminished alteration in shape and position on respiration (6). Before it becomes stretched, the pericardial sac, although full of fluid, may retain its shape, and so resemble cardiac enlargement alone (7). At first, if the effusion is not large, there may be no symptoms; later, there is dyspnœa and cyanosis. Probably at least 500 ccs. of fluid are needed to produce signs (8).

Associated with these changes in the pericardial sac, there is often massive collapse of the bases of the lungs, first on the left side and then on the right. This is an important complication and may greatly embarrass breathing. It may be due to pressure from a large effusion. It may develop before there is any effusion, and then it is possibly due to inhibition of the movements of the diaphragm. There is no question that its onset is aided by nursing patients with pericarditis lying flat. It is better to keep them sitting up.

TAMPONADE. A pericardial effusion developing quickly produces important effects in two ways; on the breathing and on the action of the heart. The space it occupies in the thorax may hinder respiration. The volume of the effusion diminishes the vital capacity and causes dyspœa (9). This may be very severe, and





PLATE 16

A
Pericardial Effusion in Myxœdema

B
The same after treatment.

To face p 84

PLATE 17



A

Hæmopericardium after Shell Wound.



B

The same showing fragment embedded in right ventricle.

cause great distress. The patient has to sit up and lean forward. He is pale and anxious. The veins in the neck are full, and there is a tinge of cyanosis in the lips, ears and nails. The pulse is rapid and weak and paradoxical. Pressure on the trachea may cause slight stridor and give rise to a dry persistent cough. Pressure on the œsophagus may lead to dysphagia. There may be acute discomfort over the precardium with a sense of suffocation. The tension on the capsule of the rapidly enlarging liver causes pain under the right costal margin.

Hæmodynamics. Study of the acute tamponade due to hæmopericardium from stab-wounds showed a low cardiac output, with raised pressure in the right auricle. The blood pressure was low, but the peripheral resistance was in the upper ranges of the normal. The high venous pressure was thought to be due to constriction of the veins, the blood volume level cannot play a part for hæmorrhage tends to reduce it. Relief of the intrapericardial pressure only caused a very slow fall in the auricular pressure; venous constriction might account for this (10) A paradoxical pulse, tending to fade on inspiration, is held to be an early sign of circulatory failure due to tamponade. It is best detected with the sphygmomanometer. The tension in the sac may interfere with the filling of the heart; the rate at which the effusion forms determines this second effect, for if it accumulates quickly the sac has not time to stretch and tamponade results. When there is a large effusion the venous pressure rises and the external jugular veins fill. After a time the liver may become engorged and ascites accumulate. The pulse is paradoxical and the blood pressure tends to fall. There is a slowing of the circulation centrally, as shown by an increase in the time taken for blood to flow from the arm to the tongue (by decholin); and at the periphery, as shown by the increased arterio-venous oxygen difference, which is indicated by cyanosis

The output of the heart has been studied in one case by modern methods (11). It was found that while the venous pressure was raised, the actual "filling pressure," that is to say, the difference between the right intra-auricular pressure and the pressure outside the heart—in this case that *inside* the pericardial sac—was within normal limits. The cardiac output was normal. When the pericardial sac was tapped the pressure in it

right auricular pressure fell pari passu, so that the filling pressur remained as before. The output of the heart remained unchanged From this it would seem that the rise in venous pressure can, u to a point, maintain the filling pressure, and allow the output t remain at a normal level At this stage, then, venesection woul do harm. Up to a certain level of intrapericardial pressure th output may be maintained. But as the effusion increases, or i the pericardial sac can stretch no more, the output will eventuall fall. The outcome depends on the volume of the effusion and th rate at which it forms, and the possibilit of the sac distending to accommodate it.

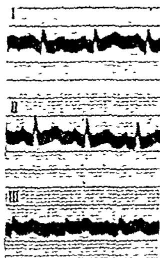


Fig 18
Low voltage in tamponade

The electrocardiogram is but littl affected in simple *serous effusion*; sometimes the voltage may be low. Alternation may appear in the curve when it is large (12). In tamponade there may be no change in the duration of systole, as shown by *measuring the* Q-T interval (13). This may help to distinguish gross enlargement where the Q-T interval may be prolonged (Fig. 18)

The effect of tamponade *is obvious* at autopsy when the left ventricle has ruptured; the heart is contracted and its chambers are empty, while the great veins are much distended.

Paracentesis. This may be needed to relieve these difficulties and may be life-saving. It is often necessary to insert a needle in order to obtain a sample of fluid for diagnosis In tuberculosis this may be valuable. The indications for tapping the pericardial sac are found in the state of the jugular veins and the degree of dyspnœa and the character of the pulse Cases of acute tamponade due to hæmopericardium from trauma need to be tapped, preferably soon, before the blood clots. Warren and others (10) found that the cardiac output then rose, the arteriovenous oxygen difference fell; the pulse became less paradoxical and the peripheral resistance fell. The question of raising the venous pressure was considered, and tried by intravenous infusion. It is interesting

to note that by this means the filling of the heart against the high intrapericardial pressure was so improved that the cardiac output and blood pressure rose, and the arteriovenous oxygen difference decreased. On the whole, paracentesis to lower the intrapericardial pressure seems preferable.

After anæsthetising the skin and subcutaneous tissues, the needle is inserted in the fifth interspace, just outside the apex beat, within the area of pericardial dullness. Some recommend the axillary line in children if the effusion is very large (14). It may be tapped in the angle between the xiphisternum and the costal margin, directing the needle upwards at an angle of 30 degrees This method is rather more difficult than the first. There is very little danger of wounding the heart, or a coronary vessel. We prefer the first method. A pyopericardium will usually need surgical drainage. Injections of penicillin should be given into the sac.

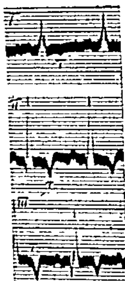


FIG 19
Permanent inversion of T-waves in a case of chronic rheumatic carditis

The Cardiogram in Acute Pericarditis. Some change appears in the cardiogram in acute pericarditis in 80 per cent of cases, and in 37 per cent it is characteristic (15). All observers agree that there is elevation of the R-T junction in all leads, especially in lead II (16) (see Fig. 17) T is exaggerated at first, later it becomes low or negative (17) (Fig 19)

These changes are transient, and may only be found early. They are particularly conspicuous in cases of purulent pericarditis of virulent type (18) There does not seem to be any association with the amount of effusion (19) except the possibility of low voltage. The changes are probably due to sub-epicardial inflammatory changes. These set up a current of injury and this causes the positive potential recorded in the R-T phase (Figs 17A and 17B).

There is some superficial resemblance to the curves of infarction, but the differences are clear. No Q-waves appear. The changes

are "concordant" in all three limb leads, not "discordant" or reciprocal in leads I and III (18). It has been suggested that diffuse pericarditis may account for certain transient atypical concordant infarction curves (20). Somewhat similar curves have been recorded in myocardial contusion (21) and following a stab wound (22). In uræmia, there are slight changes of the type due to pericarditis, when the pericarditis of the final stages appears. They are inconspicuous because the underlying myocarditis is minimal (23).

Chronic Pericarditis (Adhesive)

The long standing results of pericardial inflammation are thickening of the surfaces and adhesions. The former are often merely "milkspots," and the result of wear and tear; they are thus more common as age advances; but there seems to be some association with valvular and myocardial disease (24)

The degreee of thickening of the pericardial sac, and of the extent and density of the adhesions, both inside and outside it, vary enormously, and thus cause the diversity of opinion as to their effect on the heart and on the possibility of their diagnosis.

Clinically, fixation of a large heart is difficult to diagnose. Systolic retraction of ribs may be deceptive when a powerful right ventricle thrusts forward. Stress has been laid on this movement as a sign of adhesion, and also on some inhibition of movement seen on screening (25). It is not a reliable sign and is found without adhesions. Doubt has been thrown on the idea that extra-pericardial adhesions are responsible for hypertrophy. The accompanying valvular lesions are blamed (26). Not all authorities agree on this. The diagnosis of pericardial adhesions, even when thick, is difficult, apart from those found in cases of constriction when they can be inferred. The valvular lesions are the things that matter as far as the efficiency of the heart is concerned.

Tuberculous Pericarditis

This disease is most commonly met with in males over the age of forty years (27). The infection usually reaches the sac by the lymphatic channels from the mediastinal glands. Occasionally the sac is infected as a part of a general blood stream dissemination. Locally there may be pain and a dry cough, or the general symptoms

of wasting, fever, associated with polyserositis and peripheral stasis, may predominate (28). The onset is liable to be insidious and very indefinite (29). The disease may start with an initial acute phase, followed by a stage of effusion or caseation, and finally end in the third phase, when adhesions are formed and the sac may become constricted (30). It is possible that congestive failure may develop owing to gross thickening of the visceral pericardium (31).

Infections of the heart valves and myocardium are very rare (32). The effusion is usually serous, but may be hæmorrhagic, in this resembling that found when the sac is invaded by malignant disease. In the serous type lymphocytes predominate and tubercle bacilli may be found by guinea pig inoculation. A negative result

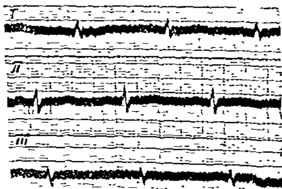


FIG 20
Low voltage curve Flat T-waves

does not exclude. Large amounts may accumulate and produce a state of [illegible] w low [illegible] the accounts the prognosis is bad, although the disease runs a very chronic course. Only 15 *per cent* of cases recover (32). Other observers give a better prognosis (29).

As the sac shrinks the syndrome of Pick may develop; this is unlikely to happen if the patient recovers, and in tuberculosis calcification is not seen. Some cases have but very slight clinical manifestations (33). When the effusion becomes large, so that the venous pressure increases, or particularly when dyspnœa appears, the sac should be aspirated (27). This may be repeated, and the

are "concordant" in all three limb leads, not "discordant" or reciprocal in leads I and III (18). It has been suggested that diffuse pericarditis may account for certain transient atypical concordant infarction curves (20). Somewhat similar curves have been recorded in myocardial contusion (21) and following a stab wound (22). *In uræmia, there are slight changes of the type due to pericarditis, when the pericarditis of the final stages appears.* They are inconspicuous because the underlying myocarditis is minimal (23).

Chronic Pericarditis (Adhesive)

The long standing results of pericardial inflammation are thickening of the surfaces and adhesions. The former are often merely "milkspots," and the result of wear and tear; they are thus more common as age advances; but there seems to be some association with valvular and myocardial disease (24).

The degreee of thickening of the pericardial sac, and of the extent and density of the adhesions, both inside and outside it, vary enormously, and thus cause the diversity of opinion as to their effect on the heart and on the possibility of their diagnosis.

Clinically, fixation of a large heart is difficult to diagnose. Systolic retraction of ribs may be deceptive when a powerful right ventricle thrusts forward. Stress has been laid on this movement as a sign of adhesion, and also on some inhibition of movement seen on screening (25). It is not a reliable sign and is found without adhesions. Doubt has been thrown on the idea that extra-pericardial adhesions are responsible for hypertrophy. The accompanying valvular lesions are blamed (26). Not all authorities agree on this *The diagnosis of pericardial adhesions, even when thick, is difficult, apart from those found in cases of constriction when they can be inferred. The valvular lesions are the things that matter as far as the efficiency of the heart is concerned.*

Tuberculous Pericarditis

This disease is most commonly met with in males over the age of forty years (27). The infection usually reaches the sac by the lymphatic channels from the mediastinal glands. Occasionally the sac is infected as a part of a general blood stream dissemination. Locally there may be *pain and a dry cough, or the general symptoms*

enlargement, however, is not uncommon and does not vitiate the diagnosis (39).

HÆMODYNAMICS. Investigation of the circulation when the sac is constricted shows that the stroke volume is diminished and the output per minute low (40). The venous pressure is increased, and infra-red photography shows great engorgement of the superficial veins; the peripheral stasis is indicated also by an increase in the arteriovenous oxygen difference. At the centre, the rate of the flow of blood from the arm to the lung is retarded, as tested by the intravenous injection of ether, which can be detected in the breath (41).

The prolongation of the circulation time appears to run parallel to the rise in venous pressure. Recent investigations (42) of the hæmodynamics of the circulation when the sac is constricted have confirmed the low cardiac output. It was found that as the rate of the heart increased the stroke volume decreased, but the minute volume of output might be raised, with some fall in the venous pressure. Increasing the venous pressure by intravenous infusion could not raise the cardiac output. The output also remained *unchanged in spite of spontaneous variations in the venous* pressure. These findings are interesting as a contrast to the effects of tamponade due to pericardial effusion. Here the venous pressure may rise, so that the right auricular filling pressure is maintained and the output kept within normal limits (11), or the inflow may be actually increased, with a corresponding rise in output (43).

The reason suggested for this difference is the fact that "the obstruction to filling is not a high pressure, which may be overcome, but a non-distensible scar which puts a limit to dilatation of the ventricle during diastole" (43).

The fluctuations in venous pressure were associated with variations in the blood volume. In congestive heart failure there is an increase in blood volume, which may in part be due to retention of sodium (44) Possibly the same cause operates in Pick's syndrome. Venous constriction must also be considered. Phlebotomy only produced a limited fall in venous pressure. The findings in acute hæmopericardium were rather similar in this respect; here hæmorrhage would tend to decrease the blood volume, so venoconstriction may be important (10).

introduction of air to form a pneumopericardium has been recom mended, in order to avoid the formation of adhesions (29). Possibl this procedure is of little practical value, as organisation inside th sac will occur in any case (34). The question of operation ma arise, in order to relieve constriction. It should be noted that th thickening of the sac may be extreme and spoil the possibility o surgical relief. Some advise operation if the sac is shrinking, eve if the disease is active. If those who recover do not usuall develop Pick's syndrome, and the prognosis is otherwise so bad it would be better not to interfere when the tuberculous proces is active. Where the sac is shrunken, operation may provid satisfactory relief. The tuberculous nature of the infection doe not debar.

Constrictive Pericarditis (Pick's Syndrome). The venous engorgement and its associated phenomena due to a constricted pericardial sac are known as Pick's syndrome (1896). The disease was well described by N. Chevers in the Guy's Hospital Reports (London) in 1842. Concato's disease, or polyserositis, may give rise to Pick's syndrome, if the pericardial sac becomes constricted. The possibility of surgical relief has attracted much attention since the paper by P. D. White in 1935 (35). In most cases the cause of the constricting process is obscure. Rheumatism does not play a part and tuberculosis is probably not common. Trauma has been recorded. In one case, after six years, it was due to a needle (36). We have seen it follow spontaneous hæmorrhage in purpura. The initial attack often causes so little disturbance that it is not noted About twelve months may elapse between the acute infection and the development of Pick's syndrome (37), or as much as twenty-nine years (38) The constricted sac hampers the diastolic filling of the heart. As a result there is a tendency for the venous pressure to rise. The congestion, for obscure reasons, is often more conspicuous in the portal system, causing gross painless enlargement of the liver, and ascites The veins in the neck become permanently full, with but little pulsation, and the distension tends to increase during inspiration, when the volume of the pulse also tends to fall (pulsus paradoxus). At the periphery there is some degree of cyanosis. The conspicuous feature is the combination of the phenomena of congestive failure with but little abnormal in the heart. A moderate degree of



PLATE 18
Calcified Pericardial Sac.

To face p 92

The blood pressure is usually low and the pulse pressure small. The heart itself shows, in contrast, remarkably little. There is no enlargement as a rule; there are no lesions of the valves But it must be remembered that a slight degree of enlargement does not exclude. The local constrictions have been known to cause stenosis of the pulmonary artery above the valves; the signs were a systolic murmur and thrill and loud second sound (45).

X-RAY FINDINGS. On screening there is diminished pulsation. The heart may appear to stand still (46). The heart remains fixed on lateral tilting of the patient, and does not elongate on the descent of the diaphragm on inspiration. The aortic knob is small and flat. The usual curves of the cardiac contour are lost. Pulling on the diaphragm by adhesions may be seen. Calcification may be visible, or show in the skiagram. It usually appears as a line inside the rim of the heart shadow. *Its relationship to the edge* may indicate the thickness of the sac. Sometimes a double line can be seen, showing layers on the parietal and visceral pericardium. The latter often extends into the muscle. *Calcification always means an obliterated sac, but there may be no venous* congestion. The heart should be viewed and photographed from all angles; the oblique aspects may show calcification best. Kymography may be helpful. The maximum reduction of pulsation is usually along the borders of the right auricle and aorta. The left border may show normal pulsation (see Plate 18).

The vital capacity is normal unless there are associated lesions in the lungs or pleuræ, such as constrictive pleurisy (47). There is no pulmonary engorgement. The electrocardiogram often shows low voltage, and usually the T-waves are flat (Fig. 21).

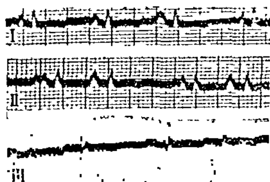


FIG 21

Pick's syndrome. Low voltage QRS. Large P waves.

Treatment. Medical treatment has little to offer. Paracentesis and diuretics cannot relieve the congestion for long;



PLATE 18
Calcified Pericardial Sac.

To face p 92

digitalis is definitely contra-indicated unless there is fibrillation (48). Resection of the pericardial sac, pericardiolysis, can cure (35) (37) and (39). How far the constriction can be relieved depends on local conditions and varies much from case to case. It should certainly be attempted after adequate preliminary treatment by removal of ascites and œdema During operation, cardiographic records may show nothing abnormal; others have noted auricular fibrillation and flutter and paroxysmal tachycardia, auricular and ventricular. All these disturbances were transient (49) (50). They may indeed occur at any operation under general anæsthesia. Quinidine as a prophylactic before operation is of little value.

The relief to the circulation, once a normal and efficient cardiac action is resumed, may be dramatic. In some cases, however, the improvement is slow. Comparison of kymograms before and after operation shows the increase in cardiac pulsation (38). The heart increases in size. The improved filling and emptying of the heart raises the output per minute and increases the stroke volume. The rate of blood flow from arm to tongue rises and the venous pressure falls. At the periphery the arterio-venous oxygen difference decreases (48)—in short, a normal circulation may be restored. There is an increase in the voltage of the cardiogram in some cases (51) Others show changes due to post-operative pericarditis (51), or little change at all (48).

A review of thirty-seven cases, of whom twenty-eight were treated with pericardiolysis, reports that fourteen were cured. Sixteen showed calcification (37).

After operation, pleurisy with effusion is common and transient fibrillation frequent It is advisable to nurse in an oxygen tent at first.

The diagnosis of these cases is not difficult once the significance of the combination of congestive right ventricular failure and an apparently normal heart is recognised. Medical treatment should aim at preparation for operation and must not be carried on too long—sudden failure may occur (52). Apart from pericardiolysis, the outlook is quite hopeless.

REFERENCES

1 Sunderland, S, Wright-Smith, R. J (1944) *Brit. Heart J*, 6, 167.
2 Cossio, P, *et al* (1942) *Amer Heart J*, 24 227
3 Barnes, A, Burchell, H (1942). *Amer Heart J*, 23, 247.
4 Nathan, D A, Dathe, R. A. (1946) *Amer. Heart J*, 31, 115

5 SCHNITZER, R, GUTMAN, D (1946). *Brit. Heart J*, **8**, 25.
6 FREEDMAN (1939). *Amer J. Ront*, **42**, 38.
7 STEWART, H J, CRANE, N F., DEITRICK, J. E (1938). *Amer Heart J*, **16**, 189
8 KEMP, P, WHITE, P. (1932). *Amer. J. med Sci*, **184**, 782
9 PALMER, H D (1937) *M R C Reports*, No. 222, Cardiac Enlargement
10 WARREN, J V, *et al.* (1946) *Amer. Heart J*, **41**, 418
11 FLETCHER, C M (1945) *Brit Heart J*, **7**, 143
12. FELDMAN, L (1938) *Amer Heart J*, **15**, 100
13. TUNG, C (1941) *Amer Heart J.*, **22**, 35
14. SUTTON (1934). *Amer J. Dis Child*, **48**, 44
15. BELLET, MCMILLAN (1938) *Arch in Med*, **61**, 381
16 VAN DER VEER, J, NORRIS, R (1937) *Amer Heart J*, **14**, 31
17. NOTH, P, BARNES, A. (1940) *Arch in. Med*, **65**, 291.
18 VAN DER VEER, J, NORRIS, R (1939) *J Amer. med Assoc*, **113**, 1483
19 OSTRORSKI, W, PINES, I (1937). *Z f ges exp Med*, **101**, 465
20 LANGENDORF, R (1941) *Amer Heart J*, **22**, 86
21. SMITH, L. B, MCKEOWN, H J (1939) *Amer Heart J*, **17**, 560
22 LANGENDORF, R, GOLDBERG, S (1942) *Amer Heart J*, **24**, 412
23 KEITH, *et al* (1946) *Amer Heart J*, **31**, 527
24. NELSON (1940) *Arch Path*, **29**, 256
25 DRESSLER, W. (1937) *Arch in Med*, **60** 654
26. PARKINSON, J (1936) *Lancet*, **1**, 1337
27. BLALOCK, A, LEVY, S (1937) *J Thoracic Surg*, **7**, 132
28. KEEFER (1937). *Ann in Med*, **10**, 1085
29 ELLMAN, P (1945) *Brit Heart J*, **7**, 147
30 HEIMANN, H L, BINDER, S (1940) *Brit Heart J*, **2**, 165
31 BARRETT, A M., COLE, D (1944) *Brit. Heart J*, **6**, 185
32. HANNESSON, H (1941) *Tubercle*, **22**, 79
33 HARVEY, WHITEHILL (1937) *Medicine*, Baltimore, **16**, 45
34. BARNWELL, ADCOCK (1940) *Hosp Bull Ann Arbor*, **6**, 1 (cit 25)
35. WHITE, P D (1935) *Lancet*, **2**, 539
36 STRAUSS, B (1944) *Amer Heart J*, **28**, 805
37 EAST, T, HUNTER, J (1939) *Lancet*, **1**, 255
38 GRISWOLD, R A (1936) *J Amer med Assoc*, **106**, 1054
39 HARRISON, M, WHITE, P D (1942) *Ann in Med*, **17**, 790
40 BURWELL, C S, HICKINGER, D (1935) *Arch in Med* **56**, 250
41. STEWART, H J, *et al* (1938) *J clin Invest*, **17**, 581
42 LYONS, R H, BURWELL, C. S (1946) *Brit Heart J*, **8**, 33
43 COOPER, F W, STEAD, F A, WARREN, J V (1944) *Ann Surg*, **120**, 822
44 LYONS, R H, JACKSON, S D, AVERY, N L, (1944) *Amer J med Sci*, **208**, 148
45 GOULEY, R (1937) *Amer Heart J*, **13** 470
46 STEWART, H, J, CARTY, J R, SEAL, J R (1943) *Amer J. Roentgenol* **49**, 349
47 BURWELL, C S, AYER, G D, (1941) *Amer Heart J*, **22**, 267
48 STEWART, H, HEUER, J (1939) *New York State J*, **39**, 2183
49 STEWART, H J, BAILEY, R L (1941) *Amer Heart J*, **22**, 169
50 FEIL, H, ROSSMAN, P (1939) *Ann in Med*, **13**, 402
51. CUSHING, E H, FEIL (1930) *Amer J med Sci*, **192**, 527
52 SHAW, C (1941) *Lancet*, **1**, 76
53. NAY, BOYER (1946) *Amer Heart J*, **32**, 222

CHAPTER III

MYOCARDIAL DISEASE

A variety of diseases are here considered shortly, because they have a common factor in that they all involve the myocardium principally, to a greater or lesser degree.

They may be classified as :—

- Cardiac Tumours (primary and secondary).
- Contusion and Trauma.
- Diphtheria.
- Myocarditis (Fiedler's type).
- Hypertrophy of obscure origin.
- Sarcoidosis.
- Trichinosis.
- Myotonia Atrophica.
- Emetine Intoxication.
- Scleroderma.
- Addison's Disease.
- Vitamin B Deficiency.

Primary Cardiac Tumours

Primary cardiac tumours are rare. They are of two types; the myxomas, which form ball valve thrombi, and the sarcomata. Fibromata also occur, but they are usually small and cause no symptoms.

Cardiac Myxoma. Cardiac myxomas always arise in the auricles, usually in the left (1). They are usually attached by a pedicle to the region of the foramen ovale. Histologically they contain few cells and it has therefore been suggested that they are organizing thrombi However, thrombi are more common in the ventricles than in the auricles and do not usually arise in them without some cause such as mitral stenosis Myxomatous rests are known to occur near the fossa ovalis, and the cells, though few, have a characteristic spindle shape (2)

5. SCHNITZER, R, GUTMAN, D (1946). *Brit Heart J.*, **8**, 25.
6 FREEDMAN (1939) *Amer J Roent*, **42**, 38
7. STEWART, H. J, CRANE, N. F., DEITRICK, J. E (1938). *Amer Heart J*, **16**, 189
8 KEMP, P., WHITE, P (1932) *Amer J med Sci*, **184**, 782.
9 PALMER, H D (1937) *M R.C Reports*, No 222, Cardiac Enlargement.
10 WARREN, J. V., *et al* (1946) *Amer Heart J*, **41**, 418
11 FLETCHER, C M (1945) *Brit Heart J*, **7**, 143
12 FELDMAN, L (1938) *Amer Heart J*, **15**, 100
13. TUNG, C (1941) *Amer Heart J*, **22**, 35
14. SUTTON (1934) *Amer J Dis Child*, **48**, 44
15. BELLET, MCMILLAN (1938) *Arch in Med*, **61**, 381
16 VAN DER VEER, J, NORRIS, R (1937) *Amer Heart J*, **14**, 31
17 NOTH, P, BARNES, A (1940) *Arch in Med*, **65**, 291
18 VAN DER VEER, J, NORRIS, R (1939) *J Amer med Assoc*, **113**, 1483
19 OSTRORSKI, W, PINES, I (1937). *Z f ges exp Med*, **101**, 465
20 LANGENDORF, R (1941) *Amer Heart J*, **22**, 86
21 SMITH, L B, MCKEOWN, H J (1939) *Amer Heart J*, **17**, 560
22 LANGENDORF, R, GOLDBERG, S (1942) *Amer Heart J*, **24**, 412
23 KEITH, *et al* (1946) *Amer Heart J*, **31**, 527
24 NELSON (1940) *Arch Path*, **29**, 256
25 DRESSLER, W (1937) *Arch in Med*, **60** 654
26 PARKINSON, J (1936) *Lancet*, **1**, 1337
27. BLALOCK, A, LEVY, S (1937) *J Thoracic Surg*, **7**, 132
28 KEFFER (1937) *Ann in Med*, **10**, 1085
29 ELLMAN, P (1945) *Brit Heart J*, **7**, 147
30 HEIMANN, H L., BINDER, S (1940) *Brit Heart J*, **2**, 165
31. BARRETT, A M, COLE, D (1944) *Brit Heart J.*, **6**, 185
32 HANNESSON, H. (1941) *Tubercle*, **22**, 79
33 HARVEY, WHITEHILL (1937) *Medicine*, Baltimore, **16**, 45
34. BARNWELL, ADCOCK (1940) *Hosp Bull Ann Arbor*, **6**, 1 (*cit* 25)
35 WHITE, P D (1935) *Lancet*, **2**, 539
36 STRAUSS, B (1944) *Amer Heart J*, **28**, 805
37. EAST, T, HUNTER, J (1939) *Lancet*, **1**, 255
38 GRISWOLD, R A (1936) *J Amer med Assoc*, **106** 1054
39 HARRISON, M, WHITE, P D (1942) *Ann in Med*, **17**, 790
40 BURWELL, C S, HICKINGER, D (1935) *Arch in Med* **56**, 250
41. STEWART, H J, *et al* (1938) *J clin Invest*, **17** , 581
42 LYONS, R H, BURWELL, C. S (1946) *Brit Heart J*, **8**, 33
43 COOPER, F W, STEAD, E A, WARREN, J V (1944) *Ann Surg*, **120**, 822
44. LYONS, R H, JACKSON, S D, AVERY, N L, (1944) *Amer J med Sci*, **208**, 148
45 GOULEY, R (1937) *Amer Heart J*, **13** 470
46 STEWART, H, J, CAREY, J R, SEAL, J R (1943) *Amer J Roentgenol*, **49**, 349
47 BURWELL, C S, AYER, G D, (1941) *Amer Heart J*, **22**, 267
48 STEWART, H, HEUER, J (1939) *New York State J*, **39**, 2183
49. STEWART, H J, BAILEY, R L (1941) *Amer Heart J*, **22**, 169
50 FEIL, H, ROSSMAN, P (1939) *Ann in Med*, **13**, 402
51 CUSHING, E H, FEIL (1930) *Amer J med Sci*, **192** 527
52 SHAW, C (1941) *Lancet*, **1**, 76
53. NAY, BOYER (1946) *Amer Heart J*, **32**, 222

CHAPTER III

MYOCARDIAL DISEASE

A variety of diseases are here considered shortly, because they have a common factor in that they all involve the myocardium principally, to a greater or lesser degree.

They may be classified as :—

- Cardiac Tumours (primary and secondary).
- Contusion and Trauma.
- Diphtheria
- Myocarditis (Fiedler's type).
- Hypertrophy of obscure origin.
- Sarcoidosis
- Trichinosis
- Myotonia Atrophica.
- Emetine Intoxication.
- Scleroderma.
- Addison's Disease.
- Vitamin B Deficiency.

Primary Cardiac Tumours

Primary cardiac tumours are rare. They are of two types; the myxomas, which form ball valve thrombi, and the sarcomata. Fibromata also occur, but they are usually small and cause no symptoms.

Cardiac Myxoma. Cardiac myxomas always arise in the auricles, usually in the left (1). They are usually attached by a pedicle to the region of the foramen ovale. Histologically they contain few cells and it has therefore been suggested that they are organizing thrombi. However, thrombi are more common in the ventricles than in the auricles and do not usually arise in them without some cause such as mitral stenosis. Myxomatous rests are known to occur near the fossa ovalis, and the cells, though few, have a characteristic spindle shape (2).

CLINICAL SIGNS. Myxomas in the left auricle cause symptoms by occluding the mitral orifice—the ball-valve thrombus—and by pressure on the openings of the pulmonary veins. Emboli may be detached from them. Three types have been described.

(1) *Simulating Mitral Stenosis.* Mitral systolic and diastolic murmurs are present, but the murmurs tend to vary with the position of the patient. There is no history of rheumatism and the symptoms have a recent onset. Death occurs suddenly from occlusion of the mitral orifice (3); or relentless, progressive heart failure sets in from pressure on the pulmonary veins with death from pulmonary œdema (4).

(2) *Ball Valve Thrombus.* This type gives a fairly characteristic clinical picture with sudden loss of consciousness on a change of position, usually on sitting up or standing. One such patient had an attack of pulmonary œdema in bed but refused to sit up (5). *At autopsy the mitral valve was blocked by the tumour which* fitted snugly into the orifice.

(3) *Multiple Emboli.* The tumour may cause no symptoms but emboli may be dislodged to various parts of the body (6). Other signs are enlargement of the heart for which no cause can be found (1). Skiagrams may show enlargement in the region of the pulmonary artery (7), or the left auricle may be enlarged backwards (8).

A syndrome of *Ball Valve Thrombus of the Right Auricle* has been described (9). The patient had mitral and tricuspid stenosis and auricular fibrillation. There was dusky cyanosis of the face and neck, and engorgement of veins of the neck with systolic pulsation. A striking variation in the severity of the symptoms was noted, as a peculiar feature, including the size of the heart in the skiagram.

SARCOMATA. These are very rare. If they involve the auricle, pulmonary œdema and the ball thrombus syndrome may occur (10). A leiomyosarcoma of the left ventricle caused progressive enlargement of the left ventricle simulating a cardiac aneurysm (11).

SECONDARY CARDIAC TUMOURS may occur through metastasis or from direct infiltration from an adjacent carcinoma, such as from a bronchus or the œsophagus. Secondary involvement of the heart may be suspected when a patient known to have a carcinoma,

particularly of the adrenals or a bronchus, develops a cardiac arrhythmia such as auricular extrasystoles or fibrillation or A-V heart block (12). One such case with infiltration involving the anterior and posterior walls of the left ventricle had a pronounced and persistent upward deviation of the ST junction both in leads II and III and in the precordial leads (13). Very extensive infiltration of the heart may occur with but little disturbance of function. Pericarditis, followed by hæmorrhagic effusion, is quite common.

REFERENCES

1 H [illegible] , 4, 103
2 F [illegible]
3 F [illegible]
4 T [illegible]
5 D [illegible]
6 B [illegible]
7 [illegible] Amer Heart J, 16, 117.
[illegible] J, 43, 243
[illegible] Heart J, 27, 858
[illegible] 26, 385
[illegible] Amer Heart J, 30, 209
[illegible] ed Sci 203, 520
13 ROSENBAUM JOHNSTON, ALZAMORA (1944) Amer Heart J, 27, 667

Contusion of the Heart

The heart may be bruised by any crushing injury of the thorax or by a severe blow over the front of the chest. A wheel of a vehicle may have passed over the chest, or the chest may have been crushed between a moving and a stationary object. Alternatively, a violent blow may have been received on the front of the chest by some heavy object such as beam, or the patient may have been flung forward against the steering wheel of a car. In the first case there are likely to be multiple injuries to the ribs or sternum. in the second there may only be a small bruise at the point of impact.

Pathological Findings. In those dying from multiple [illegible]

[illegible] ventricle (1). [illegible] commonest cause of death from a cardiac contusion [illegible] of the heart [illegible] accident (2) I [illegible] to contusion o [illegible]

acute failure, and a loud murmur, systolic in time, at the apex. Rupture of a chorda tendinæ is less serious. A ventricular aneurysm may lead to death months after the trauma (4).

Symptoms. IMMEDIATE. These vary greatly according to the associated injuries. Cardiac symptoms may be masked by shock, or by the pain of multiple fractures, or pleurisy. When contusion has taken place without skeletal injury, symptoms may be absent at first. Thus one man, who died later from a cardiac aneurysm, assisted other people from the car and changed the tyre before he was struck with violent precordial pain (4). Another had his first attack of angina while walking home two hours after his injury (5). If auricular fibrillation comes at the onset, dyspnœa is likely to be present. After a severe injury the patient may die quickly from pulmonary œdema (6).

LATER. Hæmoptysis indicates contusion at the lung. Pain and dyspnœa may develop from pericarditis, or the myocardial lesion.

Physical Signs. The pulse may be totally irregular from auricular fibrillation (7). Pericardial friction may develop later (8). Gallop rhythm has been noted (9).

PERICARDITIS. By far the most common result of a cardiac contusion is pericarditis. Friction may be heard about a week after the injury (8) (10). Electrocardiograms may also be typical. A hæmopericardium which required paracentesis was seen a day after a blow on the chest (11). Recovery was complete in a fortnight.

OTHER SEQUELÆ. Angina pectoris is not infrequent. Patency of the intraventricular septum, presumably from rupture, has been recorded (12). Mitral stenosis developed after a soldier had been buried by a shell. Many years later the autopsy confirmed trauma of the valve (13).

ELECTROCARDIOGRAPHIC ABNORMALITIES. The most frequent are auricular fibrillation, which may occur immediately after the injury, and curves denoting pericarditis: other changes include A-V heart block and flattening of the T waves (14). More rarely inversion of T suggesting infarction may occur (2). We have seen these persist for three years (Fig. 22). The patient suffered severely from angina.

Treatment and Prognosis. Most cases of contusion will clear up if the patient is kept at rest, and often the associated skeletal

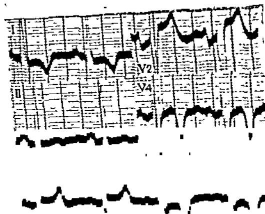


Fig 22

Angina of effort, since fracture of sternum in car accident three years before Note deep inversion of T in V_2 and V_4, also in lead I

njuries will require this. When pericarditis is present, rest should be continued until the changes in the electrocardiogram have become stationary. Angina pectoris should be treated along the usual lines

The prognosis immediately after a contusion is uncertain. Paracentesis may have to be done for hæmopericardium. There is a risk of subsequent rupture or the development of angina. The possibility of a contusion should always be borne in mind and rest in bed should be enforced in all doubtful cases. In this way some of the sequelæ could be avoided.

Penetrating Wounds of the Heart

Penetrating wounds of the heart are not often seen in this country. Electrocardiograms taken on a patient with a stab wound of the right ventricle in 1937 showed a bowed inversion of T in leads II and III (15) It was suggested that this might be due to pericarditis Recently 23 cases have been reviewed in whom serial electrocardiograms mostly with multiple precordial leads were taken from the first twenty-four hours to three years after the injury (16). Evidence of pericarditis was found in 17 cases. Leads I and II were chiefly affected in the standard leads. Eleva-

tion of S-T began during the first twenty-four hours; the T wave became inverted from the eleventh to the nineteenth day. Inversion of T might persist for three months and might mask the evidence of a right ventricular wound. However, a right bundle branch block or localized inversion of T in precordial leads furnished sufficient grounds for the diagnosis of right ventricular injury in 4 cases. Localising signs of left ventricular injury were found in 6 cases. In one the curve before operation was typical of anterior infarction, and the anterior descending branch was subsequently found to be injured. The remainder had deep inversion of the T waves in the precordial leads. Of 8 cases examined from six months to three years after the wound, electrocardiograms suggesting residual myocardial damage were found in five. The conclusion is that pre-operative evidence of cardiac involvement can be found in the majority of cases. The curves may show infarction, bundle branch block or pericarditis. After operation, changes due to pericarditis usually predominate, but evidence of local damage can sometimes be obtained from a bundle branch block or from an infarction pattern.

REFERENCES

1 Barber (1940) *Brit med J*, **2**, 520
2 Warburg (1940) *Brit Heart J*, **2**, 271
3 Glendy White (1936) *Amer Heart J*, **11**, 366
4 O'Farrell (1939) *Brit Heart J*, **1**, 172
5 Campbell (1939). *Brit Heart J* **1**. 177
6 Barber, Osborn (1941) *Brit Heart J* **3**, 127
7 Reed, Berger (1945) *Amer Heart J*, **30**, 622
8 Anderson (1940). *Brit med J*, **2**, 307
9 Sigler (1945) *Amer Heart J*, **30** 459
10 Smith, McKeown (1939) *Amer Heart J*, **17**, 561
11. Rajasingham (1939) *Brit Heart J*, **1**, 181
12 East (1945) *Brit Heart J*, **7**, 116
13 Barber (1938) *Brit med J* **1**, 433
14 Barber (1942) *Brit Heart J*, **4**, 83
15 Wood (1937) *Lancet*, **2**, 796
16 Noth (1946) *Amer Heart J*., **32**, 713

Diphtheria

The toxin of the Klebs Lœffler bacillus affects the myocardium, in addition to many other tissues. The peripheral circulation is affected as well as the heart muscle. The poison may be absorbed from cutaneous infections as well as faucial. The incidence of myocarditis may be as high as 89 per cent (1). Circulatory complications are common in severe cases and are the most important

cause of death. But nowadays the wider use of immunisation has reduced the frequency of this disease, and early diagnosis and the administration of antitoxin limits its severity when it does occur.

Myocarditis. PATHOLOGICAL CHANGES. The damage varies with the severity and duration of the infection. There may be widespread hyaline degeneration of the muscle fibres; there may be actual necrosis (1) Fibrosis shows some attempt at repair. The conducting tissues are affected as well as the rest. The valves and pericardium escape.

CLINICAL SIGNS. The heart enlarges and the apex beat becomes weak, diffuse and wavy in character. The first sound at the apex becomes weak, causing a tic-tac rhythm, or there may be a third sound causing the gallop rhythm. Changes in rate take the *form* of a pronounced tachycardia, or there may be bradycardia due to heart block. There is pallor and often vomiting, with enlargement of the liver. The systolic blood pressure may fall to 60 mm. Hg In a series of cases of cutaneous diptheria the cardiac complications came on about four to seven weeks after the infection (1)

CARDIOGRAPHIC CHANGES. Auriculo-ventricular block, partial or complete, bundle branch block (3), auricular flutter and fibrillation (4) and ventricular tachycardia all occur. There may be depression of the ST junction (6) T waves in all limb leads may become negative, and also in the precordial. Q waves may appear in CR_3 and CR_4 (1). Most of these changes are transient if the patients survive.

Complete heart block is always serious There may be Stokes-Adams attacks Complete heart-block has been known to persist. The idioventricular rhythm may be unusually fast, about 100 a minute. The block develops suddenly. The changes in the cardiogram develop early and may precede the physical signs; they may appear at the end of the first week.

If the dangers of the acute phase and convalescence are passed, the heart muscle usually recovers completely Patients examined years afterwards showed no abnormal after effects (6).

PERIPHERAL FAILURE The circulation may fail at the periphery. The blood pressure falls, about the end of the first week. There is some degree of hæmoconcentration. The patient is pale, restless

tion of S-T began during the first twenty-four hours ; the T wave became inverted from the eleventh to the nineteenth day. Inversion of T might persist for three months and might mask the evidence of a right ventricular wound. However, a right bundle branch block or localized inversion of T in precordial leads furnished sufficient grounds for the diagnosis of right ventricular injury in 4 cases. Localising signs of left ventricular injury were found in 6 cases. In one the curve before operation was typical of anterior infarction, and the anterior descending branch was subsequently found to be injured. The remainder had deep inversion of the T waves in the precordial leads. Of 8 cases examined from six months to three years after the wound, electrocardiograms suggesting residual myocardial damage were found in five. The conclusion is that pre-operative evidence of cardiac involvement can be found in the majority of cases. The curves may show infarction, bundle branch block or pericarditis. After operation, changes due to pericarditis usually predominate, but evidence of local damage can sometimes be obtained from a bundle branch block or from an infarction pattern.

REFERENCES

1 BARBER (1940) *Brit med J*, 2, 520
2 WARBURG (1940) *Brit Heart J*, 2, 271
3 GLENDY, WHITE (1936) *Amer Heart J*, 11, 366
4 O'FARRELL (1939) *Brit Heart J*, 1, 172
5 CAMPBELL (1939) *Brit Heart J*, 1, 177
6 BARBER, OSBORN (1941) *Brit Heart J*, 3, 127
7 REED, BERGER (1945) *Amer Heart J*, 30 622
8 ANDERSON (1940) *Brit med J*, 2, 307
9 SIGLER (1945) *Amer Heart J*, 30, 459
10 SMITH, MCKEOWN (1939) *Amer Heart J*, 17, 561
11. RAJASINGHAM (1939) *Brit Heart J*, 1, 181
12 EAST (1945) *Brit Heart J*, 7, 116
13 BARBER (1938) *Brit med J*, 1, 433
14 BARBER (1942) *Brit Heart J*, 4, 83
15 WOOD (1937) *Lancet*, 2, 796
16 NOTH (1946) *Amer Heart J*, 32, 713

Diphtheria

The toxin of the Klebs Lœffler bacillus affects the myocardium, in addition to many other tissues. The peripheral circulation is affected as well as the heart muscle. The poison may be absorbed from cutaneous infections as well as faucial. The incidence of myocarditis may be as high as 89 per cent (1). Circulatory complications are common in severe cases and are *the most important*

PATHOLOGICAL FINDINGS. Two types have been described. The *first* consists of granulomata, which resemble tuberculous granulomata, or gummata, but no organisms have ever been found in them. This type has been found in pregnancy and in arsenical dermatitis during treatment for syphilis. It may represent a form of allergy In the *second* there is a diffuse infiltration of the myocardium with lymphocytes, mononuclear cells, eosinophils and some polymorphs. The interstitial tissue is chiefly affected, but necrosis of the muscle fibres also occurs (2). This type may occur in infancy, and similar histological findings have been recorded in infective diseases such as pneumonia or influenza In one case hæmolytic streptococci were cultured from the myocardium (3).

CLINICAL FEATURES. The condition is hardly ever diagnosed during life. Some patients die suddenly. In others the onset of symptoms is abrupt with dyspnœa, precordial pain, restlessness and cyanosis. Death may occur from pulmonary œdema in a few days or the patient may live with a slowly progressive cardiac failure for some months. One youth complained of pain during a game, and died in fourteen hours from pulmonary œdema.

Physical signs are tachycardia, accentuation of the pulmonary second sound. Pulmonary congestion and œdema are present.

Cardiac Hypertrophy of Unknown Cause

Von Gierke's or the glycogen storage disease is one cause of massive cardiac hypertrophy in *infants*. There is enlargement of the liver and the myocardial glycogen is much increased (p. 37). Apart from this disease, cardiac enlargement has been found without any of the usual causes in two groups of cases.

1. WITH SUBENDOCARDIAL DEGENERATION There is widespread degeneration with fibrosis of the subendocardial zone. Mural thrombi are common, with infarcts in various organs. The coronary vessels are normal. On the other hand, one has seen such cases with a minimum of pathological change, even in sections. Symptoms of congestive failure with great cardiac enlargement begin in early middle age and death takes place usually within a year (4), although one case had recurrent failure over a period of thirteen years (5). Four cases have been reported

or apathetic, the pulse is fast and weak, the extremities are cold and blue. There may be no abnormal signs in the heart, clinically or in the cardiogram.

This type of peripheral failure is due to the toxæmia.

DUAL FACTORS. It is evident that in a severe infection the cardiovascular system is attacked in two ways. The peripheral failure may come on early before the myocarditis. The myocarditis developing later may be too much and death results soon. In other cases the myocardial lesions come on gradually and are severe about the fourth week; there is then danger of sudden death if the patient be allowed to get up too soon.

TREATMENT. The important thing is the early and adequate administration of antitoxin. Myocardial lesions are more common when this is given late or in too small doses. Digitalis should be avoided. Adrenalin should be used for Stokes-Adams attacks. A liberal glucose intake is indicated; there is hypoglycemia from glycolysis and the insulin secretion may be scanty.

If there has been myocarditis, prolonged rest is needed. The patient must be kept lying flat, and any exertion absolutely forbidden as long as the pulse rate is raised, or there is enlargement of the heart or weakening of the mitral first sound, or any cardiographic *abnormalities still exist*

In almost every case the recovery of the heart should be complete.

REFERENCES

1. KAY, LIVINGOOD (1946) *Amer Heart J*, 31, 744
2 CHIN, HUANG (1941) *Amer Heart J*, 22, 690
3 ALSTEAD (1932) *Quart J Med*, 1, 277
4 COOKSON (1945) *Brit Heart J*, 7, 63
5 NEUBAUER (1945), *Brit Heart J*, 7, 59
6 BULL (1945) *Amer Heart J*, 29, 704
7 ALSTEAD (1933) *Lancet*, 1, 1387

Acute Isolated Myocarditis
(*Fiedler's Disease*)

Acute isolated myocarditis was described by Fiedler in 1900. (1). The diagnosis rests upon the presence of an inflammatory process affecting only the myocardium. Neither the endocardium, pericardium, nor other structures in the body are involved to any degree. Out of 250 cases of myocarditis reviewed in 1941, fifteen were of this type (2).

Emetine. Inversion of the T wave may occur as the result of the administration of emetine. In one series of 70 cases who had received emetine hydrochloride gr. 1 subcutaneously daily for 10 days half showed either depression of the S-T interval or inversion of T. One had a bowed inversion in lead IV and precordial pain (16). In another series with a similar dosage flattening or inversion of the T in one or more leads was observed in 25 out of 32 cases (17). In eight cases the curves returned to normal within 12 days of the completion of treatment. The patients were kept in bed during the course: none had any cardiac symptoms. In yet another series a third had inversion of T in leads II and III and a quarter in lead I as well (18). The changes persisted from four weeks to four months In one case only four grains of emetine had been given: the remainder had all received seven grains or more. The hearts were not enlarged. Sometimes muscular weakness and tremor occurred, or diarrhœa and abdominal pain. It is suggested that a second course of emetine should not be given while electrocardiographic abnormalities persist, and, if any have been present, two months should elapse before it is begun.

REFERENCES

1 *Fiedler* (1900) Ueber akute interstitielle Myokarditis Reference in *Centralbl f innere Med*, 21, 212
2 [illegible] (1941) *Arch Path* 32 1000

15 [illegible] (1941) [illegible] 703

The Heart in Scleroderma

As the name implies, the outstanding lesion in scleroderma is cutaneous. The skin becomes thickened and tight, with loss of elasticity. The skeletal muscles may be affected, becoming

recently in young soldiers (5a). Electrocardiograms may show auricular fibrillation or flutter; bundle branch block or heart block (6).

Aetiology. These cases have some of the features of Fiedler's myocarditis. On the other hand, in some there were dietary deficiencies, and one had pellagra. Although thiamine was without effect, it is possible that a chronic deficiency of vitamin B plays some part in the ætiology (4).

2. WITH HYPERTROPHY ONLY. In this group the patients have died suddenly. At autopsy only gross ventricular hypertrophy has been found, without any degeneration or fibrosis. In one man who died after a lateral infarct, the heart weighed 1100 g. and the coronary arteries were widely patent (7). In another where the weight of the heart was 1350 g. the aorta was hypoplastic and it was thought there might be some pituitary dysfunction (8). A boy who suddenly fell dead had a slightly increased content of glycogen in his myocardium (9). These cases are fortunately very rare and the ætiology is quite obscure.

Sarcoidosis. Rarely in a case of generalised sarcoidosis tubercles are found in the heart and pericardium. Nine cases were collected from the literature in 1944 (10). The heart is enlarged. Electrocardiogram shows bundle branch block or complete heart block (11). Ventricular tachycardia may occur. It is possible that some cases of myocarditis of unknown origin may have been due to sarcoidosis

Trichinosis. Myocarditis is found occasionally after infection with trichina spiralis. In one case the larvæ were found in the ventricular muscle at autopsy. The T waves were inverted in leads II and III about a fortnight after infection (12).

In a large series, one fifth of the patients show abnormalities in the cardiogram. Abnormalities in the RS-T segment were often noted, and there was prolongation of QRS which tended to persist. There were no clinical abnormalities apart from those in the cardiogram (13).

Myotonia Atrophica. More than half of those suffering from this rare disease show evidence of cardiac involvement (14). Electrocardiograms show bundle branch block and latent heart block. In a few cases the heart has been enlarged (15).

Emetine. Inversion of the T wave may occur as the result of the administration of emetine. In one series of 70 cases who had received emetine hydrochloride gr. i subcutaneously daily for 10 days half showed either depression of the S-T interval or inversion of T. One had a bowed inversion in lead IV and precordial pain (16). In another series with a similar dosage flattening or inversion of the T in one or more leads was observed in 25 out of 32 cases (17) In eight cases the curves returned to normal within 12 days of the completion of treatment. The patients were kept in bed during the course · none had any cardiac symptoms. In yet another series a third had inversion of T in leads II and III and a quarter in lead I as well (18). The changes persisted from four weeks to four months. In one case only four grains of emetine had been given. the remainder had all received seven grains or more. The hearts were not enlarged. Sometimes muscular weakness and tremor occurred, or diarrhoea and abdominal pain. It is suggested that a second course of emetine should not be given while electrocardiographic abnormalities persist, and, if any have been present, two months should elapse before it is begun.

REFERENCES

1 FIEDLER (1900) Ueber akute interstitielle Myokarditis Reference in *Centralbl f innere Med*, 21, 212
2 SAPHIR (1941) *Arch Path*, 32, 1000
3 SCHERKEN, HEIBNER (1945) *Amer Heart J*, 29, 754
4 SMITH, FURTH (1943) *Arch int Med*, 71 602-619
5 FLYNN MANN (1946) *Amer Heart J* 31, 757
5a NORISS, POTE (1946) *Amer Heart J*, 32, 599
6 LEVY VON GLAHN (1944) *Amer Heart J* 28, 714
7 DOANE SEVERSKY (1944) *Amer Heart J*, 28, 816
8 COOKE, CLOAKE (1943) *Brit Heart J*, 5, 139
9 REIFENSTEIN, CHIDSEY (1945) *Amer Heart J*, 29 127
10 JOHNSON, JASON (1944) *Amer Heart J* 27, 246
11 LONGCOPE FISHER (1941) *J Mt Sinai Hosp* 8, 781
12 SPINK (1935) *Arch int Med*, 56 238
13 SOLARZ (1947) *Amer Heart J*, 34, 230
14 WARING, RAVIN, WALKER (1940) *Arch int Med*, 65, 763
15 EVANS (1944) *Brit Heart J* 6 41
16 HARDGROVE, SMITH (1944) *Amer Heart J*, 28, 752
17 COTTRELL, HAYWARD (1945) *Brit Heart J* 7, 168
18 DACK, MOLOSHOK (1947) *Arch int Med*, 79, 228

The Heart in Scleroderma

As the name implies, the outstanding lesion in scleroderma is cutaneous. The skin becomes thickened and tight, with loss of elasticity. The skeletal muscles may be affected ...

recently in young soldiers (5a). Electrocardiograms may show auricular fibrillation or flutter; bundle branch block or heart block (6).

Aetiology. These cases have some of the features of Fiedler's myocarditis. On the other hand, in some there were dietary deficiencies, and one had pellagra. Although thiamine was without effect, it is possible that a chronic deficiency of vitamin B plays some part in the aetiology (4).

2. WITH HYPERTROPHY ONLY. In this group the patients have died suddenly. At autopsy only gross ventricular hypertrophy has been found, without any degeneration or fibrosis. In one man who died after a lateral infarct, the heart weighed 1100 g. and the coronary arteries were widely patent (7). In another where the weight of the heart was 1350 g. the aorta was hypoplastic and it was thought there might be some pituitary dysfunction (8). A boy who suddenly fell dead had a slightly increased content of glycogen in his myocardium (9). These cases are fortunately very rare and the aetiology is quite obscure.

Sarcoidosis. Rarely in a case of generalised sarcoidosis tubercles are found in the heart and pericardium. Nine cases were collected from the literature in 1944 (10) The heart is enlarged. Electrocardiogram shows bundle branch block or complete heart block (11). Ventricular tachycardia may occur. It is possible that some cases of myocarditis of unknown origin may have been due to sarcoidosis.

Trichinosis. Myocarditis is found occasionally after infection with trichina spiralis. In one case the larvae were found in the ventricular muscle at autopsy. The T waves were inverted in leads II and III about a fortnight after infection (12).

In a large series, one fifth of the patients show abnormalities in the cardiogram. Abnormalities in the RS-T segment were often noted, and there was prolongation of QRS which tended to persist. There were no clinical abnormalities apart from those in the cardiogram (13).

Myotonia Atrophica. More than half of those suffering from this rare disease show evidence of cardiac involvement (14). Electrocardiograms show bundle branch block and latent heart block. In a few cases the heart has been enlarged (15).

Addison's Disease

Disease of the suprarenal glands induces profound changes in the circulation. Adrenal cortical tumours cause hypertension, either persistent or paroxysmal, and this may lead to congestive heart failure. In Addison's disease the heart is small, and the blood volume is low. Both may decrease suddenly in the adrenal crisis. The cardio-thoracic ratio was found to be always below .40 in Addison's disease, and to fall below .32 in crisis. After treatment it rose to an average of .44 (1).

In the treatment of cases with desoxycorticosterone acetate the size of the heart varies with the dose of D.O.C.A., if the daily intake of sodium is kept constant, and vice versa. If the dose of sodium in grammes multiplied by the dose of D.O.C.A. in milligrams is kept between 37 and 45, the size of the heart will remain constant (2). Thus the same effect is obtained by giving 4 grammes of sodium and 10 mg. of D.O.C.A., as by giving 8 grammes of sodium and 5 mg. of D.O.C.A. In crisis or impending crisis the dosage can be exceeded for a few days, and the product of the sodium and D.O.C.A. doses may be allowed to reach 110. Thus 5.5 g. of sodium and 20 mg. of D.O.C.A. may be given or 11 g. of sodium and 10 mg. of D.O.C.A. This dose must be reduced if the cardio-thoracic ratio reaches 0.5. The size of the heart was found to be most reliable criterion of the results of treatment. A gain in weight, if rapid, may be due to intoxication. The blood pressure may be normal even though cardiac failure is impending. The level of the blood sodium is unreliable. Nausea, vomiting, faintness, weakness and low blood pressure may recur during treatment: the size of the heart will show if an increase in the dose is needed to clear them up. The frequent estimation of the size of the heart in such ill patients is, however, not easy, and hardly practicable.

The effects on the circulation of an overdose of D.O.C.A. was investigated by giving 20-50 mg. intramuscularly to normal subjects daily for a fortnight (3). Their weight increased, due to retention of water, and so did the transverse cardiac diameter. In most the height of the T-wave was lowered, and in those who received the highest dose it became inverted. Both exercise and the injection of adrenaline enhanced the changes in the T-waves.

hardened, stiff and wasted. The term dermatomyositis may th
be used. Raynaud's phenomenon is seen in the fingers. In one ca
of dermatomyositis the vascular lesions were so severe that ulc
formed on the fingers and feet (1). The lungs may become fibro
and a stricture may form in the lower part of the œsophagus.

Cardiac Lesions. These are of special interest. In t
myocardium there is active vascular fibrosis (2, 3). The collag
fibres proliferate freely and the muscle fibres disappear. The lo
of the muscle is the important thing (5). There is some lymphocy
infiltration. Macroscopically the myocardium looks brownish a
stringy and feels flabby. The chambers are dilated. The corona
arteries and their branches are normal. A progressive heart failu
results, with normal rhythm. A gallop rhythm is heard (4, 5
The cardiogram shows low voltage, slurring of QRS and flatten
T waves. There may be heart block (4, 5). The skiagram sho
generalised cardiac enlargement.

The rigidity of the skin and thoracic muscles interferes wi
breathing and aggravates the dyspnœa. The development
œdema is hampered by the rigid, inelastic skin, and so gre
discomfort arises. The course progresses to a fatal ending a
treatment avails nothing. The point of cardiological interest
the progressive development of heart failure which is the ultima
cause of death. The course of the disease may be anything fro
a few months to a year or more.

SUMMARY. In this type of case the pathological process was th
same in all muscles. It has been suggested that scleroderm
dermatomyositis, Libman-Sacks disease and polyarteritis nodos
have all something in common (3). The histology of the last seem
to be different. Transitional and intermediate cases are met wit
Until more is known about the cause, the matter is speculative, bu
the point is worth keeping in mind. Possibly cases with myocardi
lesions will be found without scleroderma, just as the Libman
Sacks syndrome may appear without lupus erythematosus.

REFERENCES

1 [illegible] *Heart J*, 30, 441
2 [illegible] 749
3 [illegible] 43
4 [illegible] *J*, 33, 366.
5. [illegible] 67

3 Raab (1942) *Amer Heart J*, 24, 365
[illegible]

[illegible] Sci, 199, 769

Vitamin B Deficiency

The Beriberi Heart. Beriberi, as seen in the East, takes two forms, the dry with polyneuritis or encephalopathy, and the cardiovascular or "wet" form. Cardiovascular beriberi is seen in three grades of severity. Mild cases have only dyspnœa and palpitation; moderately severe cases have enlargement of the heart with œdema. In "Shoshin" the patient has severe retrosternal or epigastric pain and restlessness: there is venous congestion and œdema; the failure rapidly becomes fatal (1). This type is not seen in this country.

Beriberi is due to a deficiency of vitamin B1 (aneurin), and so affects particularly rice eating communities. In the West deficiency may be due to poverty with a grossly deficient diet (2), but it is more often seen in chronic alcoholics, who lose all desire for food and live on the calories contained in the large quantity of alcohol they consume

Clinical Features. The constant feature of all cases is œdema and cardiac enlargement. The œdema may be limited to the legs but sometimes involves also the face and abdomen, simulating *renal œdema* (3) In addition to the enlargement of the heart, which may be predominantly right-sided (8), skiagrams show prominent lung roots and evidence of pulmonary congestion. Patients may complain of dyspnœa or epigastric pain. Gallop rhythm with tachycardia is common. If the patient does not rest, venous and hepatic engorgement may ensue with [illegible]

[illegible] electrocardiogram may be normal, but flattening or inversion of the T wave may be present in one or more leads. In one case they were inverted in all three leads (6). In another series the P-R interval tended to be abnormally short,

Two cases of Addison's disease received a serious overdose. (4). Both patients developed hypertension, œdema of face and legs, pleural effusion or pulmonary œdema. The venous pressure was raised. The heart shadow was enlarged. The electrocardiogram showed low voltage curves and flat T waves. The cardiac failure disappeared after the D.O.C.A. had been reduced and the patient had received full doses of digitalis.

In Addison's disease sodium is lost from the body and so the blood volume falls. *The small heart is due to the loss of cellular* glycogen and water (2). D.O.C.A. allows the sodium to be retained, and so the balance is restored. Potassium seems to be lost from all muscle tissues, and especially from the heart, after prolonged treatment with D.O.C.A. It is advisable to give between 5 and 7 grammes daily during treatment.

In overdosage with D.O.C.A. the blood volume rises and cardiac failure with œdema develops. Very much the same changes were observed in the normal subjects who were given D.O.C.A. as in another group who took excess of salt in their diet. It is possible, therefore, that the suprarenals play some part in the increase in blood volume which takes place in cardiac failure from other causes.

Potassium. The effect of potassium upon the electrocardiogram has been noted in several conditions. When given as potassium citrate and chloride to normal subjects the height of the T wave increased (5). The action seemed to be through the vagus. Flat and inverted T waves in myxœdema became upright after taking potassium (6). In *familial periodic paralysis* the T waves were flattened when the patient was in an attack with complete flaccid paralysis (7). They became normal when recovery took place following the administration of 8 g. of potassium chloride. Flattened or inverted T-waves were found in patients who had taken too much D.O.C A., as well as in the normal subjects who were given it. It would seem likely that these changes are due to loss of potassium, although it should be remembered that flattened T waves occur in a number of other conditions which bear no relation to Addison's disease.

REFERENCES

1 McGavack (1941). *Amer Heart J*, 21, 1
2 McGavack (1942) *Amer Heart J*, 24, 99.

3 RAAB (1942) *Amer. Heart J*, 24 365
4 CURRENS, WHITE (1944). *Amer Heart J*, 28, 611
5 THOMSON (1939) *Brit Heart J*, 1, 269
6 SHARPEY SCHAFER (1943) *Brit Heart J*, 5, 85
7 STEWART, SMITH, MILHORAT (1940) *Amer J. med Sci* 199, 789

Vitamin B Deficiency

The Beriberi Heart. Beriberi, as seen in the East, takes two forms, the dry with polyneuritis or encephalopathy, and the cardiovascular or "wet" form. Cardiovascular beriberi is seen in three grades of severity. Mild cases have only dyspnœa and palpitation; moderately severe cases have enlargement of the heart with œdema. In "Shoshin" the patient has severe restrosternal or epigastric pain and restlessness: there is venous congestion and œdema; the failure rapidly becomes fatal (1). This type is not seen in this country.

Beriberi is due to a deficiency of vitamin B1 (*aneurin*), and so affects particularly rice eating communities. In the West deficiency may be due to poverty with a grossly deficient diet (2), but it is more often seen in chronic alcoholics, who lose all desire for food and live on the calories contained in the large quantity of alcohol they consume

CLINICAL FEATURES. The constant feature of all cases is *œdema and cardiac enlargement*. The œdema may be limited to the legs but sometimes involves also the face and abdomen, simulating renal œdema (3) In addition to the enlargement of the heart, which may be predominantly right-sided (8), skiagrams show prominent lung roots and evidence of pulmonary congestion. Patients may complain of dyspnœa or epigastric pain. [illegible]

[illegible] these cardio-vascular signs [illegible]

[illegible] of the heart has been noted (5). There was perivascular œdema with separation of the muscle bundles.

ELECTROCARDIOGRAM. The electrocardiogram may be normal, but flattening or inversion of the T wave may be present in one or more leads In one case they were inverted in all three leads (6). In another series the P-R interval tended to be abnormally short.

below 0.14 second in 5 out of 9 cases. In several there was right axis deviation, as one might expect (8).

Circulatory Changes. Patients have been noted to have warm skins. The pulse pressure may be raised, with pistol shot diastolic sounds. The velocity of the blood flow was rather fast (5). These observations suggest that the cardiac failure may be of the type with high output, and confirmation by means of the auricular catheter will be awaited with interest.

Summary. Deficiency of vitamin B1 (aneurin) causes cardiac failure with œdema. If the patient does not rest, venous congestion and severe dyspnœa may ensue. The cardiac failure is never so severe in those whose capacity for exertion has been limited by peripheral neuritis. *There is some evidence that the failure may be of the high output type*, but confirmation of this by modern methods is at present lacking.

Treatment. Digitalis is useless. Rapid and complete recovery may be expected on 10 to 20 mg. of crystalline aneurin given intra-muscularly thrice daily. Yeast should be taken by mouth. The cardiogram returns to normal, the heart regains a normal size. The therapeutic effect of aneurin, adequately administered, is so reliable as to be diagnostic. The prognosis is therefore good, once the diagnosis is made.

Pellagra is due to deficiency of vitamin B2. There is a characteristic dermatitis and pigmentation of the exposed parts of the skin, paræsthesia and mental dullness. Out of 27 cases 18 showed some flattening of the T waves with slight depression of the S-T interval (7). The changes returned to normal after treatment with nicotinic acid. A case with the dermatitis of pellagra, peripheral neuritis, and œdema has been described. The T waves were inverted (5). There was no dietary deficiency and the condition was ascribed to mal-absorption.

REFERENCES

1. Wenckebach (1934) "Das Beriberi Herz," Vienna
2. [illegible] (1940) *Brit. Heart J.* 2, 241
3. [illegible] *rt J.*, 1, 187.
4. [illegible] *eart J.*, 2, 231
5. [illegible] *ed. Assoc.*, 109, 786.
6. [illegible] *ancet*, 1, 738.
7. [illegible] *Heart J.*, 7, 72.
8. [illegible] *Quart. J. Med.*, 15, 91.

CHAPTER IV

HYPERTENSION

Essential Hypertension

The classical definition of hyperpiesia, or primary, essential hypertension, which Sir Clifford Allbutt gave to his original description was "a disease which, independent of the kidneys has its own characters, of which high arterial pressures, both systolic and diastolic, seem to be the chief." A vast amount of research during the last twelve years has done much to incriminate the kidneys to a degree hardly suspected at first. The claim to independence in the initial stage has still to be refuted.

This disease of the civilised peoples has a high incidence nowadays. In the United States it causes something over one-third of the total deaths (22) Well may it now usurp from tuberculosis the title from John Bunyan used by Osler, "Captain of the Men of Death."

The Normal Blood Pressure. The range of the normal is wide, not only from patient to patient, but from time to time, and in various parts of the arterial tree. There may be as much difference as 10 mm. systolic and 5 mm. diastolic between the pressures in each brachial artery (1).

Age Variations. The range of the normal varies with age. According to Wiggers (4), up to sixteen years the systolic pressure tends to rise from 90 to 115, and the diastolic from 65 to 75. At forty the upper limit of normal is 140 systolic and 90 diastolic. Above this age the systolic may reach 150, but the diastolic should not exceed 90. The systolic pressure is, of course, labile, but in some subjects the diastolic too may vary considerably with emotion.

Posture. Standing up causes a fall in the systolic of 10 to 20 mm., and a slight rise in the diastolic of 5 to 10 mm. The systolic should slowly regain its usual level in a minute or so.

Technique. If readings are to be reliable one cannot pay too much attention to the minutiæ of technique Whether the patient sits or lies makes but little difference (3). The standardization of

technique has been defined by the joint recommendations of the Cardiac Society of Great Britain and Ireland and the American Heart Association (4). It is worth while to note certain points that should be emphasised. The rubber bag should be 12 to 13 cm. wide and must be fitted closely over the brachial artery. The mercury should be raised rapidly 30 mm. above the level at which the radial pulse ceases to be felt and then allowed to fall about 3 mm. per second. The level at which the sounds are first heard gives the systolic pressure, unless the palpatory level is the higher; in which case it is taken. There may be some variation on respiration; when there is arrhythmia, such as fibrillation, the reading can only be approximate. When there are premature systoles the large returning beat should be disregarded. If the arm is fat, bulging of the cuff should be avoided or the reading will be inaccurate. Occasionally the sounds fade below the systolic level, and an "auscultatory gap" is present. Reading the returning sounds at the lower limit of the gap as the systolic pressure will be avoided, if the palpatory method is used first. Both pulses should be felt, and the pressure read in both arms if they appear to be unequal. The diastolic pressure should be read at the point when the sounds suddenly become dull and muffled. The American Committee suggested that the level at which the sounds disappear indicates the diastolic. This may be several millimetres below the point of change. In aortic regurgitation, thyrotoxicosis, and sometimes in nervous patients, the sounds may persist unchanged right down the scale. In this country the point of change is accepted as the diastolic pressure. That this is accurate enough for ordinary purposes has been shown by a graphic instrumental method (5). On the other hand direct intra-arterial readings suggest that the auscultatory method gives a systolic which is some 10 mm. too low, while the diastolic agrees with the point at which the sounds disappear (fifth phase) rather than *the level of change (fourth* phase) (6). If the point of change does not agree with the point at which the sounds disappear, the three figures may be recorded. It is clear that neither level is free from objections. In the majority of cases the difference between the two is too small to matter.

Femoral Readings. The relative heights of the pressures in the femoral and brachial arteries have been studied. The muscular mass of the thigh would indicate the use of a larger cuff than one

12 cms. in width; 15 cms. is suggested. Some observers think that with the patient prone the usual cuff is adequate (7). They find that the systolic pressure in the leg is some 35 mm. higher than in the arm and the diastolic 25 mm. Standing up increases the diastolic pressure considerably. Others prefer the wider cuff: with the narrow one the indirect readings, compared with a direct method, are 17 per cent inaccurate for the systolic and 58 per cent for the diastolic pressures. With the larger cuff the systolic gives only a small error: *the diastolic is too high* (8).

In taking femoral readings, as has been stated, a cuff 15 cms. wide, with a cover longer than usual, is probably best. The patient should be prone and the bell of the stethoscope placed over the popliteal artery. The systolic and diastolic readings can then be made fairly accurately. Further confirmation by other observers of the higher pressures shows that the systolic and diastolic readings are about 35 mm. and 20 mm. higher than in the brachial (9). Undue venous congestion from *prolonged reading* may raise the diastolic pressure (10).

It is always important to eliminate as far as possible, emotional disturbances, and allow the pressure to settle down. *Aneroid* manometers are apt to get out of order.

Factors Causing Variations. *The Basal Pressure.* When the person is truly at rest, mentally and physically, the basal pressure may be surprisingly low, often below 100 mm. in Europeans (11). During sleep the pressure may fall to 95. The *term* "supplementary pressure" has been used for the difference *between the* "basal pressure" and the "*casual* pressure," which represents the reading obtained without special *relaxation*.

The systolic pres…

Meals may cause

may cause a grea

pressures. *Emo*

… considerably, but sometimes the diastolic rises too. Nervousness may abolish the change in the sounds which should show the diastolic pressure. *Alcohol* tends to cause a *fall* in pressure. *Tobacco* (nicotine) causes a rise in pressure in some people (12). *Climate.* The pressures of Europeans tend to be rather *lower* in hot climates and warm weather. *Respiration* causes rhythmic variation. The pressure tends to fall on inspiration and rise *on* expiration. This is mainly

because there is a lag in the effect produced by the increased filling of the right heart on inspiration, so that the resulting increase in the output of the left side does not show itself until the succeeding expiration (2).

It is apparent that a single reading of the blood pressure does not give more than limited information. The more observations that can be obtained the better, owing to the rather wide variations from many causes. The limits of the normal are not precise. *Many consider that 100 mm. may be regarded as the* upper level for the diastolic, rather than 90. But as there is some disagreement, amounting to as much as 10 mm. at which point the reading should be made, and in many instances the end point, particularly at phase 4, is not clear-cut, a dubious or border-line case may have to be assessed *on additional findings and* several readings taken. One thing is certain; they will all be different.

Diagnosis of Essential Hypertension. The diagnosis in the early stages is not easy. One has become accustomed to regard a reading of over 160/100, as abnormally high. One definition has given 150/90, when found *consistently*, as indicative of hypertension (13). The important word is "consistently"; for the range of variation, considering age, sex, race, and emotional state, is not small. It is clear that one reading is of but little value, and the more that can be made the more meaning they have. The basal pressure is definitely raised in hypertension: as the casual pressure rises, so the basal is increased as well. The supplemental pressure has a variable level, for the casual and basal pressures vary independently (14). If circumstances allow, the true basal pressure should be obtained The higher the basal pressure the more is the casual likely to be raised (15). There is no doubt that the early phases of essential hypertension are marked by transient rises, and when *the diastolic pressure is recorded over 100 it is very significant* (16). Emotional instability affects the systolic pressure chiefly, and with a diastolic at normal level a raised systolic can then be disregarded. When the pressure tends to be high, it is most important to gauge the patient's nervousness. The rate of the heart may be a guide, but it is not always raised. The increase in the force of the heartbeat is probably as useful an indication as any other.

Cold Pressor Test. In order to detect possible latent

hypertension or evaluate border-line cases, the cold pressor test of Hines and Brown (17) has been extensively tried. The hand is immersed in ice-cold water for a minute, and the pressure measured in the other arm. A rise of over 20 mm. Hg. in the systolic and 15 mm. Hg. in the diastolic has been regarded as a hyper-reaction. Hypertensive persons gave rises of 40 mm. or more.

As an indication of a "pre-hypertensive state" the test has various interpretations Russell (18) found that there was no relation between hyper-reaction and the subsequent development of hypertension. In persons over the age of fifty the test had but little use, for about half the apparent normals gave positive results (19). The same conclusion had been previously reached by Feldt and Weinstrand (20) Other observers have found the results so variable on different occasions on the same subjects that the definition of "normals" and "hyper-reactors" was impossible (21, 22) In spite of these variable results it would appear that hypertensives are twice as likely to react as normals. A positive reaction is not given in nephritis (23). This also has been found by another observer (24). There is no doubt that the test shows a measure of vasomotor instability, and may suggest that the cause of essential hypertension is already present (25). One-third of these hyper-reactors developed hypertension within six years, while none of the hypo-reactors did It has been possible to demonstrate a familial tendency to hyper-reaction.

There is some evidence that prolonged immersion in cold sea-water may lead to the development of subsequent hypertension, although it is difficult to exclude some predisposition (26)

The conclusion would be that hyper-reactors are more likely to develop hypertension than normals. But normal reaction does not exclude hypertension later, nor does hyper-reaction make it inevitable It is difficult to base a diagnosis on hyper-reaction in any individual case. The early diagnosis must depend on taking into consideration as many factors as possible The ætiological points that must be borne in mind are dealt with next

Aetiology. There are clearly many predisposing or partial causes of essential hypertension even if the true and final one still awaits discovery.

RACE. It appears that negroes in Africa have lower pressures than those in America. The Chinese have lower pressures than

Europeans. But questions of diet, local disease, climate and so forth, come in too. *Crossing with the white race seems to increase* the incidence of hypertension in American negroes. In the United States the incidence among them may be higher than in the white population (27, 28).

Sex. There seems to be a higher incidence among women but figures vary.

Age. The frequency of essential hypertension increases over the age of forty. From this age onwards the incidence mounts steadily, particularly among women. Between the forty and forty-nine 26 per cent were males and 32 per cent females. Between fifty and fifty-nine 41 per cent were males and 53 per cent females (29).

Heredity. *The general impression is that there is a strong* familial incidence. One investigation showed that when both parents had normal tension, only 2.1 per cent of the children had raised pressures. When both parents had hypertension, the incidence among the childern was 45.5 per cent (30). In another series there was a family history of hypertension in 87 per cent of cases. The incidence was six times greater when the family history *was positive in another group, than when it was negative* (13).

In a recent study there was found to be a family history of hypertension in about four-fifths of the cases. The hypothesis was advanced that this is a "hereditary" disease conveyed as a Mendelian dominant with a rate of expression of more than 90 per cent (30a)

Individual Diathesis. That a plethoric type exists, with a tendency to overweight and thick-set build, in whom high blood pressure is common, few will deny. While obesity is not a cause of hypertension, it is often an associated finding (31). It must be remembered that a fat arm may lead to a falsely high reading with the ordinary cuff. When patients were divided into two types, tall and thin "linear," and thickset or "broad," it was found that in the "linears" the ratio of low pressure to high was as three to one; while in the "broads" *it was as one to three. In any* random group of male "broads," the high pressures were thrice as common as the low, and five times as common in females. In any random group of hypertensives the "broads" were as four to one among the males, and eleven to one among the females (32).

Although the classification into the two types may not be very accurate, the figures are striking and confirm personal impressions. Whatever may be the method that starts the hypertensive state, the underlying causes seem to be psycho-somatic and of genetic origin, buried deep in the stuff of the stock from which the individual springs (32a).

ENDOCRINE CAUSES. It is very doubtful whether menopausal hypertension exists. The association is probably fortuitous, as there is a tendency for hypertension to develop about the time of the menopause in any case. In normal women, as in men, the graph of the average increase in the blood pressure readings between the ages of twenty and sixty follows a straight line. There is no tendency for the pressure to rise unduly in women between the ages of forty and fifty (33) There may be an association with hyperthyroidism (34), and hyperthyroidism may precipitate hypertension; but removal of the bulk of the thyroid does not alleviate the hypertension (35). The raised basal metabolic rate so often found in hypertension is obscure in origin. The thyroid is normal, and partial thyroidectomy does not reduce the raised metabolism (36). The clinical features of pituitary and adrenal tumours are discussed elsewhere (p. 135).

RENAL ISCHÆMIA. When Goldblatt (37) produced hypertension in dogs by clamping both the renal arteries, or clamping one artery and removing the kidney on the other side, the very important conclusion became clear that renal ischæmia *might lead to* hypertension. Later Page (38) showed that *constriction* of a kidney by a cellophane envelope produced *similar* results. The next step was to eliminate all possibility that nervous influences led to the rise in pressure. Denervation of the kidneys (39), resection of the splanchnic nerves (40), destruction of the spinal cord (41), sympathectomy (42), interfered in no way with the rise in blood pressure. The inference, then, was that there was a humoral cause, for nervous factors had been excluded; that some substance was produced in the ischæmic kidney *that had* a pressor action. As the pressure did not rise when the renal vein [illegible]

[illegible] kidney into the neck of a dog whose kidneys had been removed, for a rise in blood pressure at once

Europeans. But questions of diet, local disease, climate and so forth, come in too. Crossing with the white race seems to increase the incidence of hypertension in American negroes. In the United States the incidence among them may be higher than in the white population (27, 28).

Sex. There seems to be a higher incidence among women but figures vary.

Age. The frequency of essential hypertension increases over the age of forty. From this age onwards the incidence mounts steadily, particularly among women. Between the forty and forty-nine 26 per cent were males and 32 per cent females. Between fifty and fifty-nine 41 per cent were males and 53 per cent females (29).

Heredity. The general impression is that there is a strong familial incidence. One investigation showed that when both parents had normal tension, only 2.1 per cent of the children had raised pressures. When both parents had hypertension, the incidence among the childern was 45.5 per cent (30). In another series there was a family history of hypertension in 87 per cent of cases. The incidence was six times greater when the family history was positive in another group, than when it was negative (13).

In a recent study there was found to be a family history of hypertension in about four-fifths of the cases. The hypothesis was advanced that this is a "hereditary" disease conveyed as a *Mendelian dominant with a rate of expression of more than 90* per cent (30a).

Individual Diathesis. That a plethoric type exists, with a tendency to overweight and thick-set build, in whom high blood pressure is common, few will deny While obesity is *not a cause* of hypertension, it is often an associated finding (31). It must be remembered that a fat arm may lead to a falsely high reading with the ordinary cuff. When patients were divided into two types, tall and thin "linear," and thickset or "broad," it was found that in the "linears" the ratio of low pressure to high was as three to one; while in the "broads" it was as one to three. In any random group of male "broads," the high pressures were thrice as common as the low, and five times as common in females. *In* any random group of hypertensives the "broads" were as four to one among the males, and eleven to one among the females (32).

Although the classification into the two types may not be very accurate, the figures are striking and confirm personal impressions. Whatever may be the method that starts the hypertensive state, the underlying causes seem to be psycho-somatic and of genetic origin, buried deep in the stuff of the stock from which the individual springs (32a).

ENDOCRINE CAUSES. It is very doubtful whether menopausal hypertension exists. The association is probably fortuitous, as there is a tendency for hypertension to develop about the time of the menopause in any case. In normal women, as in men, the graph of the average increase in the blood pressure readings between the ages of twenty and sixty follows a straight line. There is no tendency for the pressure to rise unduly in women between the ages of forty and fifty (33). There may be an association with hyperthyroidism (34), and hyperthyroidism may precipitate hypertension; but removal of the bulk of the thyroid does not alleviate the hypertension (35). The raised basal metabolic rate so often found in hypertension is obscure in origin. The thyroid is normal, and partial thyroidectomy does not reduce the raised metabolism (36). The clinical features of pituitary and adrenal tumours are discussed elsewhere (p. 135).

RENAL ISCHÆMIA. When Goldblatt (37) produced hypertension in dogs by clamping both the renal arteries, or clamping one artery and removing the kidney on the other side, the very important [illegible]

[illegible] envelope produced similar results. The next step was to eliminate all possibility that nervous influences led to the rise in pressure. Denervation of the kidneys (39), resection of the splanchnic nerves (40) destruction of the spinal cord (41), sympathectomy (42), interfered in no way with the rise in blood pressure. The inference, then, was that there was a humoral cause, for nervous factors had been excluded; that some substance was produced in the ischæmic kidney that had a pressor action. As the pressure did not rise when the renal vein was occluded, it appeared that the pressor substance left the kidney in the blood (43). The presence of the pressor substance in the renal vein was shown by transplanting an ischæmic kidney into the neck of a dog whose kidneys had been removed, for a rise in blood pressure at once

resulted (44). Further, the presence of a pressor and vasoconstrictor substance has been demonstrated in the blood from an ischæmic kidney (45) and also in the plasma of hypertensive patients (46).

Thus it became clear from experiment that the ischæmic kidney was the source of a pressor vasoconstrictor substance, and that, also, a healthy kidney could in some way eliminate it. Removal of a healthy kidney causes no rise in blood pressure; subsequent constriction of the main artery of its fellow does. After the initial rise following unilateral constriction of a renal artery, the pressure slowly tends to fall; if the healthy kidney is removed it rises again (45). The source and the fate of the pressor agent was shown to be in the kidneys.

THE PRESSOR SUBSTANCES. Page (47) showed that renin was liberated from the ischæmic kidney. When injected into normal animals it reproduced the hypertension caused by the ischæmia of Goldblatt's clamps (48). Renin is a protein, a pseudo-globulin, a proteolytic enzyme (49). It may be formed in the renal tubules, near the afferent glomerular artery (50). It has been demonstrated in extracts from the ischæmic kidney (51). The amount present in the blood is roughly proportional to the rise in blood pressure (52). It resembles pepsin, by which it can be replaced. A pressor substance can be formed by the action of pepsin on renin activator (53). Before it can act as a pressor substance it must be activated by a substrate, which is present in the plasma. The substance with which renin reacts is a heat-labile, non-dialyzable pseudo-globulin which has been called "renin-activator" (Page) or "pre-angiotonin" (Goldblatt) or "hypertensinogen" or "prehypertensin" (54)

It is formed in the liver and is present in the plasma as part of α_2 globulin. Its formation depends on the secretion of adrenalin (55), for it disappears from the blood when the suprarenals are removed. The result of this enzyme reaction is a thermostable, crystalline substance, a polypeptide, *angiotonin* (56), or *hypertensin* (Braun-Menendez). The total amount of angiotonin formed depends on the amount of the globulin substrate, for the quantity of renin needed is quite small. There is an increased amount of preangiotonin (prehypertensin) present in the blood in animals with experimental ischæmic hypertension, and also in the blood of patients with essential hypertension (57)

Action of Angiotonin (Hypertensin). The intravenous injection of angiotonin causes a rise in blood pressure in normal persons; there is vasoconstriction and blanching of the skin (58). The action is apparently a direct one on the muscle coats of the arterioles (59). On the isolated mammalian heart angiotonin causes constriction of the coronary arteries and diminution of the diastolic volume, with increase in the oxygen consumption and in the amplitude of the beat (60).

The effects of angiotonin on the kidneys are important. There is a decrease in the rate of the flow of blood through the kidneys resulting from vasoconstriction in the renal arterioles. If the vasoconstriction predominates in the arteriole efferent from the glomerulus the pressure in the glomerulus will rise (61). The result is that the glomerular filtration will not be decreased. The conclusion is that efferent glomerular constriction predominates. The effects of the intravenous injection of angiotonin have been worked out on normal human beings. They are those of essential hypertension. The systolic and diastolic pressures are raised, with an increase in the pulse pressure. The renal blood flow is decreased, but the rate of glomerular filtration is unchanged, indicating constriction of the arteriole efferent from the glomerulus (62, 59).

Investigation of the renal function of hypertensive patients shows that a similar state of affairs is present in them (63). Clamping the renal artery in patients has caused the release of renin, thus provoking the renal humoral pressor mechanism (64).

The conclusion is that a rise in blood pressure develops on a change in the blood flow in the kidney, because of the formation of a vasoconstrictor substance angiotonin (hypertensin) by the reaction of an *enzyme*, renin, liberated from the kidneys, on a *substrate*, preangiotonin (hypertensinogen), formed in the liver. Angiotonin can reproduce most of the circulatory phenomena found in essential hypertension, but it has not yet been isolated from the blood of patients with this disease. In fact, there is a suggestion that [illegible]
the plasma c[illegible]
of the hype[illegible] the matter still awaits conclusive evidence.

Sensitivity to Angiotonin. The question arises whether there may be an abnormal degree of sensitivity to angiotonin

(hypertensin). There is no experimental evidence to support this (57), but the possibility has not been excluded in hypertensive patients. This side of the question must not be forgotten and might play a part in pathogenesis. Nervous or endocrine causes may facilitate this action, or that of some similar substance (66)

ELIMINATION OF ANGIOTONIN. Goldblatt showed that when one kidney remained intact the blood pressure in ischaemic hypertension *tended to fall* to normal. The inference was that the healthy kidney was in some way responsible, for the pressure rose again on its removal (67). Excretion of renin could not be the reason, as the renal threshold for it was too high (68). Moreover, an uretero-venous fistula revealed no excretion of pressor substance (69). It was found, however, that normal serum would destroy angiotonin in vitro, and Braun-Menendez (70) has suggested that an enzyme "hypertensinase" (Angiotonase) might be responsible. The renal cortex contained more of this substance than any other tissues, and removal of both kidneys caused its disappearance from the blood. The conclusion is that a healthy *kidney provides the means for controlling the amount of the* pressor substances. As a cause for hypertension the possibility remains of an increase in the pressor substance or a decrease in its destroyer. The possibility of angiotonase providing therapeutic effects remains to be seen. That a deficiency of angiotonase might cause hypertension is unlikely. It is present in the same amount in hypertensive patients, normal persons, and even in patients with Addison's disease (71).

THE METHOD OF PRODUCTION OF RENAL PRESSOR SUBSTANCES. It would appear that it is not really the reduction in the actual quantity of blood flowing through the kidney that leads to the *liberation of renin. A change in the* character of the flow is probably the important point (72) The important change may be a reduction in the pulse pressure in the kidney. The actual *flow may not be much diminished. The main thing is the fall in* filtration pressure in the glomeruli. The important point may be that there is change from a pulsatile flow to a continuous flow (73). The brilliant work at the *Nuffield* Institute at Oxford by Trueta and others has recently shown that the circulation of the blood through the kidney can be

cortex. Here lies a possible cause of

diversion of blood is probably a natural function upon which the manifold chemical activities of the kidney depend. Its misuse may set in action the pressure mechanism of hypertension. This humoral cause may be at first due to reversible physiological dysfunction, perhaps of neurogenic origin; later on there set in irreversible pathological changes (73a).

Conclusions. The experimental work of the last twelve years has carried knowledge a considerable step forward in the problem of essential hypertension, even if the final solution is still wanting. The production of renin must have an object, if one takes a teleological view. It appears when it is necessary to "maintain the head of pressure in the glomeruli, upon which glomerular filtration depends" (74). This is a vital matter; the kidneys are important organs which receive one-quarter to one-third of the cardiac output. It is noteworthy that hæmorrhage leads to renin production by reducing blood pressure (75) The release of the pressor renin leads to the formation of angiotonin which further causes vasoconstriction in the renal arterioles. If the renal angiotonin mechanism is originally a necessary beneficent mechanism, it may become harmful, presumably from some such vicious circle. It is still obscure how the circle starts. The discovery of the dual circulation in the kidney may prove to be the long-sought key to this problem. The prospect of a further great advance in the understanding of the pathogenesis of hypertension may well be unfolding.

Unilateral Renal Lesions. A direct result of Goldblatt's discovery is the recognition of the possible rôle of unilateral renal lesions in the causation of hypertension. A variety of pathological conditions have been described. Obstruction of the main renal artery by atheromatous plaques is not uncommon (76, 77, 78, 79). The question arises whether these were *present before* the pressure rose, or whether they were rather the result of the hypertension.

Tuberculosis; *pyelonephritis*, usually with hydronephrosis, and tumours have also been *reported* In deciding whether operation is advisable, the following points must be considered (80).

1. The onset of [illegible]
2. The tot [illegible]
3. The ren [illegible] e function of the kidney

The presence of retinal lesions does not debar. Those cases are probably a good deal less common than was first supposed. The diagnosis based on the pyelogram is apt to be fallacious (22). Some writers are very sceptical of the association in clinical medicine between unilateral renal lesions and hypertension. This view is shared by Homer Smith (81). There are many cases of such lesions where no high pressure results. Surgical removal of the suspected kidney may not relieve the hypertension. Some cases reported have not been followed long enough (82). An interesting observation has been made that after operation there may be an improvement in the function of the remaining kidney; for it has been possible to demonstrate an increase in the flow of blood and an increase in the filtration rate (83).

There are, however, a number of well authenticated successful cases on record where unilateral nephrectomy has cured. Even when the hypertension has reached a malignant phase operation may meet with success (84). Unfortunately, the great majority of hypertensives do not fall into this category. High blood pressure was not found more frequently in a series of patients with surgical disease of the kidneys than in a comparable series without it (22). Rare though the reported instances may be, the possibility is worth bearing in mind when a severe degree of hypertension is found unexpectedly in a young person who has no evidence of nephritis. It is well worth while to carry out an intravenous pyelography in all younger patients, particularly when there is any history of renal or urinary symptoms, and when there is no record of hypertension in the family. If need be, retrograde pyelography can then be done (85a). The risk of failure largely depends on whether the remaining kidney has developed the arteriolar lesions consequent on prolonged hypertension.

Hæmodynamics of Hypertension. The rise in pressure characteristic of essential hypertension affects the diastolic, and to a still greater degree the systolic, so that the pulse pressure is increased.

Mechanism. There is no increase in the viscosity of the blood in hypertension, nor is there any increase in the output of the heart. Modern methods with cardiac catheterisation and the ballistocardiograph have confirmed this (22). Eliminating these

causes, the third remains; increase of *peripheral resistance*. The increase in peripheral resistance is general throughout the arterial system (85), and appears to be due to increase in the arteriolar tone (86). Study of the pressure gradients shows that the resistance is in the smaller arterioles (87) It has been shown that there is an increase in the resistance of the digital arteries, while the flow still remains normal, as a result of the raised pressure (88). There is no evidence that pathological changes in the arterial system occur early enough to be the cause of increased resistance. The vasoconstriction can be eliminated. Vasodilatation can be induced by heat and reactive hyperæmia (89). Pyrogenic agents can restore the blood flow to normal in hypertensive kidneys, and cause the blood pressure to fall and the peripheral resistance to decrease (63) The vasomotor reactions show that the nerves are active, but the response is no more than is met with in normal people. Nerve block and sympathetic block give no greater increase in flow in hypertension. The excessive vascular tone is presumably due to a humoral and not to a nervous cause.

THE PULSE PRESSURE. The raised diastolic pressure is due to the high peripheral resistance. The excessive height of the systolic pressure, giving a high pulse pressure, may be due to changes either in the elastic arteries, with some degree of contraction of the larger arteries (90), or to a change in the distensibility of the aorta resulting from the high diastolic pressure (91).

The cardiac output remains unchanged, but the beat increases in force

There is no change in the cerebral blood flow (92).

RENAL ARTERIOLES Much attention has been paid to the question of the degree and site of the vasoconstriction of the renal arterioles and its effects on glomerular and tubular function. Constriction of the arterioles afferent to the glomerulus will reduce the total flow through the kidney, thereby reducing the filtration through the glomerulus and the excretory function of the tubule. The ultimate effect is a balance between the tendency of the level of the blood pressure to increase the flow and the constriction to obstruct it. Constriction of the arteriole efferent from the glomerulus will raise intraglomerular pressure and so increase filtration, but it will at the same time render the tubule ischæmic and diminish tubular excretion. If afferent constriction pre-

dominates glomerular pressure falls; if efferent, then it rises. Both reduce total flow. Goldring and others (63) have investigated the renal hæmodynamics in hypertensive patients, analysing the glomerular and tubular functions by inulin and diodrast. They have found that early in the disease there is a decrease in the effective renal blood flow. This is due to increase in the tone of the arterioles efferent from the glomeruli. The increased efferent tone can be eliminated by fever and by vasodilatators. Increase in afferent glomerular arteriolar tone might, it is true, have the same effect, but it has not been demonstrated at this stage. Early in the disease the filtration fraction (that is to say the quantity of plasma filtered at the glomerulus in relation to the total renal plasma flow) is found to be increased, as shown by *inulin clearance. A rise in the glomerular pressure would tend to* increase the actual amount of plasma filtered; this would be certainly due to an increase in the efferent arteriolar tone; since it is found that, despite the decrease in flow, the actual amount of filtration remains within normal limits, increase in efferent arteriolar tone must surely be present. This increase in tonus is part of the generalised vasoconstriction. There is, early in the *disease, a tendency to a decrease in the functional excretory* capacity of the tubules, as shown by diodrast excretion. It seems likely that this is due to ischæmia resulting from constriction in the efferent arteriole of the glomerulus. Denervation does not abolish the increased arteriolar tone. It must be humoral in origin. Angiotonin can produce the same effect. The pressor vasoconstrictor substance in hypertension still awaits identification (22). Nevertheless *the ischæmic state of the tubule may set in motion the* renin-angiotonin mechanism; but how does it start? Page and Corcoran (1) stress the possibility of a neurogenic cause which may operate in the earliest phases. At this stage the pressure is variable, manifestly from nervous influences. They suggest that these cause general vasoconstriction, including the afferent glomerular arterioles. The balance between the rise in pressure and the *vasoconstriction at this point will leave the function of* the nephron, glomerular filtration and tubular excretion unaffected. The constriction of the afferent arteriole at first protects the glomerulus from the raised pressure. If in some of the renal bed afferent vasoconstriction predominated, so that the renal flow fell,

or the constriction tended to lower the intrarenal pulse pressure, then the humoral mechanism might be set in action (74). There would then be efferent glomerular arteriolar constriction as a result, with further aggravation of its cause. To have a chemical regulator acting over a long period of time must be important in the control of such an important organ as the kidney. It is tempting to suppose that in essential hypertension we have a normal mechanism which has in some way become perverted.

The dual circulation in the kidney as demonstrated by Trueta and others may play a part. The nature of the early changes in the circulation within the kidney is still uncertain, but the solution seems likely to be found here.

Pathological Changes. That these are the result and not the primary cause of essential hypertension is now generally agreed. As a result of increased tonus the muscular coats of the arterioles throughout the body hypertrophy. The internal elastic lamina becomes multiplied many times; the intima shows hyperplasia which may become the site of slower hyaline or more acute fatty necrosis. The distribution of these changes in the various organs varies. The skin is relatively immune, and so is the gastrointestinal tract, the muscles are variable; the heart is affected occasionally; the kidneys are affected always; the spleen in about two-thirds and the liver in about a third (93). The relative proportion in which media or intima may be affected varies in different organs and in individual organs (94). The intimal proliferation and degeneration is seen at its severest in the kidney The obliterative effect is of the greatest importance, particularly as it affects mainly the arterioles afferent to the glomerulus. Lesions similar to those have been widely produced as a result of experimental hypertension (95).

Changes in Individual Organs. *The Heart.* The muscle fibres of the left ventricle undergo hypertrophy. The bulk of the heart is greatly increased. In the early phases there is typical concentric hypertrophy; later the chamber dilates. The septum may bulge into the right ventricle and interfere with its filling. (Bernheim's syndrome.) (p. 132).

Dilatation of the right ventricle comes in the later phases. Degenerative changes in the myocardium are relatively slight in many cases if the coronary arteries have escaped atheromatous

obliteration and the arterioles intimal hyperplasia, as they may do in 40 per cent of cases (96). They may be absent even when heart failure has resulted. Sometimes coagulative necrosis of the myocardial fibres, fatty degeneration and new fibrous tissue are seen, which are perhaps due to anoxæmia (97). It has been suggested that the thickened fibres are too large for the efficient diffusion of oxygen through them and so they fail to meet the extra demands made upon them. Actually there is a relative shortage of capillaries per unit of area. But the very large, thick fibres have *scalloped edges, giving an increase of the surface through which* oxygen may diffuse. The work done depends on the diastolic length of the fibres; hypertrophy of the fibres does not continue to increase indefinitely as a response to diastolic stretching; when this stretching (dilatation) ceases to be a stimulus to hypertrophy and ability for more work, it is harmful. Although the coronary arteries may hypertrophy to a certain extent, they often fail to supply blood adequately to these large ventricles, even when they are free from atheroma. The development of this particular limitation in the blood supply at once introduces baleful effects. It is probably more common in hypertensive patients than in normal persons. Apart from precipitating failure, it leads to angina pectoris, which may be provoked more easily in these large hearts with high demands, by a lesser degree of atheromatous obliteration (98).

The Kidneys. The initial findings are obliterative processes in the arterioles, particularly those afferent to the glomeruli, and hypertrophy of their muscular coats. The obliterative process varies in rate and intensity and the histological findings are in accord. The rapid process is more cellular and liable to acute degeneration and necrosis; *the slower is more hyaline, with more* phases of successive proliferation of the elastica. The glomeruli whose blood supply is interfered with degenerate and become *hyaline and fuse with their capsules.* The tubules atrophy and disappear. Fibrosis marks their end. The distribution of the changes is patchy: some nephrons are still intact and may be hypertrophied. Perhaps the distribution of these final lesions might suggest the point put forward elsewhere, as to the possible "patchy" incidence of physiological dysfunction at the onset.

Ultimately the renal blood flow may become greatly diminished, so that the glomerular filtration and tubular excretion are far below normal. Urea retention marks the final stages of breakdown. All these changes come relatively late and are found of course in the post-mortem room. Renal biopsy in the operating theatre, on the other hand, has shown that in about half the patients submitted to sympathectomy the kidneys were practically normal (99).

The Vicious Circle. Although it is clear that the early phases of essential hypertension are in the nature of a physiological derangement, or perhaps the aberration of a normal process, the cause of which is as yet unknown, the persistently high levels of the blood pressure produce pathological changes in the arteriolar system as a whole, and in that of the kidneys in particular. Wilson and Byrom (95) have produced lesions in the renal arterioles of rats by inducing ischaemic hypertension. The hypertension persists after removing the clamps. The lesions closely resemble those found in essential hypertension. The blood flow through these arterioles must be reduced. The hypertension would thus produce vascular lesions which would cause renal ischaemia and so further aggravate the hypertension. A vicious circle is thus set up Some such process as this may underlie the chronic and relentless course of established hypertension, and chronic Bright's disease as well; and may well be responsible for the development and course of malignant hypertension in which renal lesions dominate the picture, and ultimately determine the fatal end. But there may be other factors, for the renin content of the blood in ischæmic hypertension may become normal after a time (100). Perhaps local increase of sensitiveness may render the action excessive

Clinical Features. A Prehypertensive Phase. The concept that a prehypertensive phase may exist has attracted a good deal of discussion. It has always been a question whether the transient rises in pressure seen from time to time are indications of a permanent increase later on. The introduction of the cold pressor test of Hines and Brown was supposed to throw some light on these tendencies Unfortunately the results of this test seem to be too erratic to provide definite indication. No doubt nervous reaction is the important factor, to such varying stimuli as

excitement, fear, pain, cold and so forth. The basis here is neurogenic. It is well known that the level of the blood pressure is very variable at first in persons who ultimately develop true hypertension. Whether a true prehypertensive phase can as yet be differentiated from a labile blood pressure due to nervous influences is doubtful. The physical habitus, family history, and temperament may give some guidance. But we cannot for certain distinguish physiological instability of the blood pressure in persons who will not in the future develop hypertension, from those reactions in persons who may have a tendency to react abnormally to some unknown factor, and who are liable to develop pathological changes in the arteriolar system later on as a result. One investigation (13) showed that nearly three-quarters of persons with transient rises of both pressures developed a permanently raised pressure later.

Course of the Disease. The course of the disease varies enormously in its rate and degree of severity from patient to patient. In order to appreciate the phases through which it passes it is convenient to define three not very distinct stages which merge imperceptibly one into another.

The First Stage. In the early phases there are really no symptoms. The high pressure is often discovered by chance. The pressure is variable, tending to fall to normal levels at first, and during sleep. There are no abnormal signs. This may be regarded as the first phase.

Second Stage. The Cardiovascular System Reacts. The first gradually passes into the second phase. There is now definite hypertrophic thickening of the middle coats of the palpable arteries so that they assume the well-known "whipcord" character. The retinal arterioles show slight variation in calibre, with increase in light reflex.

There is an increase in the loudness of the aortic second sound, and perhaps of the mitral first sound. The apex beat may be slightly increased in force. The skiagram may as yet show no definite enlargement of the left ventricle. This first becomes manifest in an increase in the fulness of the upper part of its curve seen from the front so that it shows a rounded border with some degree of prolongation. Enlargement is also seen early in the left anterior oblique position. The electrocardiogram is normal in the

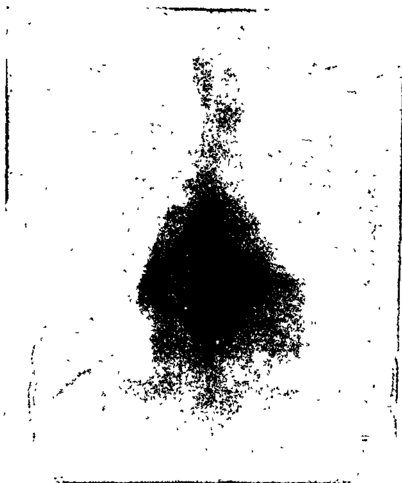


PLATE 19

Longstanding Hypertension.

Note appearance of enlarged left ventricle.

To face p. 129

standard leads, but chest leads may show changes earlier. The pressure is still variable, but definitely and permanently higher, the readings are from 190 to 170 systolic and 105 to 115 diastolic. The urine is normal. There are still no definite symptoms. The patient complains of vague headache, throbbing in heart or arteries, giddiness at times. But such symptoms are often found with normal pressures, and many have no symptoms at all. This phase corresponds to group 2 of Wagener and Keith (101) The five year mortality is 30 per cent.

Third Stage. The Cardiovascular System Wears Out In group 3 these authors place patients with definite retinopathy. The five year mortality is 80 per cent. The heart becomes enlarged and the aorta "unfolds," showing elongation, and elevation, with prominence of the "knuckle." Albuminuria may be present. The electrocardiogram shows left axis deviation. Ophthalmoscopic changes are important, for the retinal arterioles are the only ones available for examination. (Plate 19)

RETINAL CHANGES. These are important and may be graded thus. First comes irregularity in calibre; then increase in the light reflex. Later compression of the veins where the arterioles cross them, increasing in degree. Then thin narrow arterioles often in a state of spasm. After this are seen hæmorrhages, and sharp white areas of exudate.

Gross hypertensive retinopathy is marked by almost bloodless vessels, soft areas of œdema, hæmorrhage and finally, most serious of all, papillœdema.



FIG. 23

From a woman of 52 with hypertension

ELECTROCARDIOGRAPHIC CHANGES. When the left ventricle enlarges, the heart *comes* to lie more obliquely. This causes deviation of the electrical axis to the left, as shown by a high R in lead I, and a deep S-wave in lead III, the former being more than +12 mm. and the latter more than -5 mm. (Barnes). As the degree of left axis

deviation increases, the S-wave in lead II becomes deep 2 of Barnes) (102) (Fig. 23).

Minor grades of left axis deviation are found in norm which are lying transversely owing to a high left dom diaphragm. Since left axis deviation is essentially d increased obliquity of the heart, it will not be shown in th where, for any reason, the heart lies more v than normal. The most common cause f a secondary right ventricular hypertroph the increase in pulmonary pressure when ventricle weakens, or to the advent of fibrillation. Other less important causes are bronchitis and emphysema with a low dia or a long narrow chest. In these cases, p leads are needed.



FIG 24
Curve of left ventricular enlargement.

PRECORDIAL LEADS. Left ventricular p erance, or hypertrophy, is shown in the p *leads by diminutive R-waves and deep S* usually exceeding 12 mm. in the leads to t of the precordium (V1 and V2), as well as R-waves to the left of the precordium (V5 The transitional point, where the R- and are approximately equal, shifts to the left. changes are independent of the position heart, and so are unaffected by any accom right ventricular hypertrophy. Multiple pr leads furnish a much more accurate pic left ventricular hypertrophy than the limb

INVERTED T-WAVES. Later changes negativity of the T-wave (Fig. 24). This *in lead I, and V4, V5 and V6 (see Fig. 8* advanced cases the negative T-wave may lead II, and the RS-T junction is depresse conception of "ventricular strain" has forward lately, one reason being that changes may regress after sympathectomy This intr a physiological as well as an anatomical cause. T_1 neg is said to be associated with left ventricular str curves of this pattern. T_2 negativity may show more

strain A certain number of cases do not show the expected pattern. One cause may be parallel changes affecting the right ventricle. Cases of Bernheim's syndrome may not show it. Robb and Robb (103) think that these patterns of left ventricular strain are due to faulty conduction from stretching of the sinospinal and bulbospinal muscle bundles. As enlargement progresses there is slight prolongation of QRS. Finally the QRS may show lower voltage as well as slurring. Left bundle branch block is not uncommon in hypertension. Recent studies (104) (Evans, *et al*) suggest that T-wave changes are due to a combination of causes, hypertrophy with ischæmia, dilatation, increased work and metabolism; and perhaps also rotation of the heart on its longitudinal and transverse axes

The cause of inversion of T_2 is still a matter of doubt. While these authors found it in a considerable proportion of hearts of normal size, another observer (105) found invariable enlargement

There seems to be some association between ophthalmoscopic changes and electrocardiographic abnormalities (106). They seem to run fairly parallel in the degree in which they may be present. It must be remembered that sooner or later disease in the coronary arteries may cause changes in the curve; in any case there may be degenerative changes in the myocardium At present so many factors are involved, it is not possible to give clear-cut conclusions.

Final Phases. The end of hypertensive patients tends to be failure of the left ventricle in about 60 per cent of cases, cerebral catastrophe in some 15 per cent, and renal failure in rather under 10 per cent (22).

LEFT VENTRICULAR FAILURE The phenomena are those of failure from any lesion by which the left side of the heart is overloaded Dyspnœa on exertion gradually progresses in intensity and is followed by attacks of breathlessness at rest, usually nocturnal The serious signs are gallop rhythm and alternation of the pulse During paroxysms of cardiac asthma, the systolic pressure often rises. but as the heart weakens the systolic tends to fall, with diminution of the pulse pressure. In the early phases the pulmonary circulation bears the brunt. The rate of the circulation through the lungs is slowed. Congestion of the pulmonary

veins can be seen on screening, and the pulmonary second sound increases in loudness.

Bernheim's Syndrome (1910). Occasionally the signs of venous and hepatic engorgement with œdema set in early with insignificant dyspnœa, the lungs remaining clear. The suggestion was that the *interventricular septum, bulging into the cavity of the right* ventricle, which is small, interfered with its filling. The hypothesis *seems to be correct. It is curious that in these cases there may be* absence of left axis deviation, although there is no enlargement of the right ventricle to neutralise it (107). The early onset of signs of right ventricular failure in a case of hypertension, or any other condition affecting the left ventricle, with relatively clear pulmonary field suggests the syndrome (107a).

THE BRAIN. Cerebral symptoms are indefinite in the early phases. As the disease progresses some patients complain of headache, vertigo, and loss of mental capacity, but many have none. Finally may come cerebral thrombosis or hæmorrhage. The final catastrophe is often preceded by transient vasomotor disturbance.

Hypertensive Encephalopathy. A great variety of symptoms are noted. There may be severe headaches, intense at times, nausea and vomiting; transient blindness and paraesthesia about the body; motor disturbance such as aphasia and paresis; or, most dramatically, severe epileptiform convulsions. Loss of memory and coma may supervene. The onset is often very sudden, but the changes are transient and recovery is complete. The blood pressure tends to rise before the attack (93) and the pressure of the cerebrospinal fluid is abnormally high (108). The local cause is cerebral angiospasm, which is part of the general vasoconstriction. Sooner or later the permanent damage of hæmorrhage *or thrombosis almost invariably follows these transient disturbances, but the interval is sometimes surprisingly long.*

SPECIAL FEATURES. *In a disease with such widespread effects* special points arise in the clinical aspects.

Coronary Artery Disease. *The association of coronary disease* and consequent myocardial infarction is not uncommon in hypertensives. *There is no doubt that these patients are more prone to* angina pectoris due to a minor degree of coronary sclerosis. There is also a tendency to a *higher incidence of coronary artery disease*

in hypertensives (96) Rupture of the heart appears to be more likely in moderate hypertension, when the wall of the left ventricle is not much thickened (109). Apart from this, the subsequent blood pressure in cases of hypertension after coronary occlusion has no influence on the longevity, or on the occurrence, duration and severity of failure (110).

MITRAL STENOSIS. It seems incongruous to find mitral stenosis and hypertension together. The course of mitral stenosis is so often run before the age is reached at which that of hypertension begins. They are both more common in women. Possibly there is no association between them, and there is no effect of hypertension on mitral stenosis, or vice versa (111).

THE KIDNEYS. As has been noted, biopsy of the kidneys in hypertension may shew little pathological change until late in the disease A trace of albumen, with a tendency to low specific gravity and nocturia is all that one meets with in many cases. The decline in renal function, as estimated by the excretion of urea and sodium chloride, in hypertensive patients is thrice that of normal persons as age advances (112). In some elderly patients a gradual uræmia comes on, sometimes precipitated by heart failure.

Malignant Hypertension. In patients between thirty-five and fifty five a grave and steadily progressive renal failure may come on with fatal results Males are more commonly affected than females (113). As regards the pathology, it seems likely that the difference between this syndrome and benign hypertension lies in the degree of severity and the rapidity of the development of the lesions in the kidneys. The high pressure causes acute necrosis of the subintimal tissues of the afferent glomerular arterioles. It is curious that in some cases renal functions are apparently not impaired at first (114) Albuminuria is not always found early (115). Some authors, however, stress early profuse albuminuria and hæmaturia (22). The experimental work of Goldblatt (116) has suggested that the typical necrotic lesions of the arterioles did *not* develop until there was renal excretory insufficiency. These discrepancies may depend on how early the diagnosis is made. Usually the diastolic pressure is excessively high. Papillœdema is the most constant early finding (Ellis). When the patient has been under observation prior to these

developments it becomes clear that the whole course of the disease has altered, and suddenly and rapidly changed for the worse. Headache becomes intense; severe abdominal pains are not uncommon. Cases seen at first in the malignant phase may be hard to differentiate from chronic nephritis. It would appear that in these patients there is a peculiar susceptibility of the endothelium of the renal arterioles to high pressure, so that renal insufficiency rapidly develops, and the vicious circle of Byrom and Wilson is soon established, with the progressive intensity of a spiral. The prognosis is almost invariably bad. Most patients die within a year of diagnosis and some within a few weeks.

Prognosis. Apart from these cases of malignant type where the picture of renal failure comes on fast, the outlook for most patients with hypertension is relatively good. In a disease which passes through such varying stages over so long a period of time it is very difficult to be precise. Although naturally the raised blood pressure is the central point, it is in many ways the least important; for it is upon the associated points, in particular the way in which the cardiovascular system stands up to it, that the prognosis is based. *Women appear to tolerate hypertension better than men.* The physical type and family history may suggest a favourable or unfavourable outlook. The habits, mode of life and temperament may be for good or bad.

In most patients the disease will run its course, but the stage in its progress at which it is discovered, and the tempo of advance is variable from patient to patient. It is necessary to assess how far the disease has advanced and how fast it is advancing in order to gauge how far it has to go. Appearing early in life the course may be more rapid. In people over fifty-five the expectation of life may be little less than the normal so benign is the course. Once heart failure has come on, two years is usually the limit, but there are many exceptions. Rarely the blood pressure falls to a much lower level as age advances; the disease seems to die out. Cerebral vasomotor disturbances indicate the liability to hæmorrhage, but it may be remote and not inevitable, as in the case of Dr. Samuel Johnson. Estimation of the *capillary fragility* with the sphygmomanometer bag (Rumpel-Leedes test) may be a guide to the liability to hæmorrhage (117). But the petechiæ so pro-

duced may be due to other causes, such as deficiency in Vitamin C (ascorbic acid)

High Blood Pressure in Certain other States. In addition to essential hypertension it will be worth while to consider certain other conditions in which high blood pressure is conspicuous.

COARCTATION OF THE AORTA. Formerly it was supposed that the blood flow distal to the obstruction was normal. The high pressure proximal to it was thought to be, in a sense, compensatory. Actually the diastolic pressure in the femoral artery has been shown by direct estimation to be as high or higher than that in the arm (118). Examination of the renal function shows that the renal flow is reduced, while the glomerular filtration rate is normal. This finding suggests constriction of the efferent arteriole from the glomerulus (119) Thus the possibility of a humoral factor arises, although Pickering (86) showed that elimination of the nervous control allowed the blood-flow in the skin of the hand to return to normal It is clear that more information is needed here, which, perhaps, observations before and after surgical operation may supply.

The systolic hypertension of the old is due to aortic sclerosis; that of aortic incompetence to increased output, polycythemia may sometimes account for raised pressure through raised viscosity; it is by no means a constant association.

ENDOCRINE DISORDERS The most conspicuous are tumours of the *suprarenal bodies*, these may be medullary, the *phæochromocytomas* or *paragangliomas* These tumours secrete an excess of adrenalin (120) The peculiar symptoms are at first attacks of malaise, fear, palpitation, sensation of precordial constriction, headache, tremor, very profuse sweating, nausea and vomiting and salivation These disturbances may be nocturnal (121) Heat is ill tolerated The B.M.R. may be considerably raised (122). Investigation of the blood flow in the skin has shown diminution as a result of vasoconstriction due to adrenalin. The rectal temperature is proportionately a little raised (123). The blood pressure rises suddenly to very high levels. Between the attacks it may be normal Bending the trunk may precipitate an attack or palpation of the abdomen Later the pressure tends to be set permanently high. Death may occur from acute failure of the left ventricle or cerebral hæmorrhage or an intense encephalopathy The attacks

developments it becomes clear that the whole course of the disease has altered, and suddenly and rapidly changed for the worse. Headache becomes intense; severe abdominal pains are not uncommon. Cases seen at first in the malignant phase may be hard to differentiate from chronic nephritis. It would appear that in these patients there is a peculiar susceptibility of the endothelium of the renal arterioles to high pressure, so that renal insufficiency rapidly develops, and the vicious circle of Byrom and Wilson is soon established, with the progressive intensity of a spiral. The prognosis is almost invariably bad. Most patients die within a year of diagnosis and some within a few weeks.

Prognosis. Apart from these cases of malignant type where the picture of renal failure comes on fast, the outlook for most patients with hypertension is relatively good. In a disease which passes through such varying stages over so long a period of time it is very difficult to be precise. Although naturally the raised blood pressure is the central point, it is in many ways the least important; for it is upon the associated points, in particular the way in which the cardiovascular system stands up to it, that the prognosis is based. Women appear to tolerate hypertension better than men. The physical type and family history may suggest a favourable or unfavourable outlook. The habits, mode of life and temperament may be for good or bad.

In most patients the disease will run its course, but the stage in its progress at which it is discovered, and the tempo of advance is variable from patient to patient. It is necessary to assess how far the disease has advanced and how fast it is advancing in order to gauge how far it has to go. Appearing early in life the course may be more rapid. In people over fifty-five the expectation of life may be little less than the normal so benign is the course. Once heart failure has come on, two years is usually the limit, but there are many exceptions. Rarely the blood pressure falls to a much lower level as age advances; the disease seems to die out. Cerebral vasomotor disturbances indicate the liability to hæmorrhage, but it may be remote and not inevitable, as in the case of Dr. Samuel Johnson. Estimation of the capillary fragility with the sphygmomanometer bag (Rumpel-Leedes test) may be a guide to the liability to hæmorrhage (117). But the petechiæ so pro-

who already has essential hypertension, her prospects are not impaired by the pregnancy. Actually there is slight temporary increase in renal blood flow. The acute specific toxæmia is of course excluded. Antecedent hypertension is not prone to provoke it (130).

Hypertension in Acute Nephritis. Pickering (131) has shown that removal of the vasomotor control improved the flow of blood in the hand. This is in favour of a nervous vasoconstrictor origin, and not a humoral for the hypertension. Observations on reflex vasodilatation measured by heat elimination have supported this idea (132).

In *chronic nephritis* there is vasoconstriction which cannot be eliminated by removal of the nervous vasomotor control (86). The difference between the casual and the basal pressures is less than in essential hypertension. The vessels are in fact less reactive to vasomotor impulses (133). The renal hæmodynamics are similar to those of the later stages of essential hypertension. The humoral mechanism is predominant. The progressive character of the disease is aided by the vicious circle of Byrom and Wilson. The importance of the level of the blood pressure as an indication of the course the disease is taking has been noted (118).

The later stages of hypertension with renal involvement may be hard to distinguish from chronic Bright's disease, unless the cases have been seen early. The relatively late appearance of papillœdema in nephritis is important (115). Usually there is more profuse albuminuria and rather a lower blood pressure and less cardiac involvement. The end is uræmia, but more insidious than the rapid course of malignant hypertension (134 135).

The hypertension of polycystic disease of the kidneys is probably similar to that of chronic Bright's disease.

[illegible] t there is a [illegible] not [illegible] psychological [illegible] foremost the [illegible] prevented from developing a "pressure-phobia." Too much attention to the blood pressure sets up a bogey worse

may continue for years. The level of the potassium in the blood may be raised; sugar and albumen may be found in the urine. The differential diagnosis from neurogenic crises of hypertension may be difficult. Attention to the history should arouse suspicions, on which the tumour must be sought for. If it is found, an exploratory laparatomy will be needed, for removal will cure. Adrenalin should be given after operation (124).

Cortical Suprarenal Tumours, adenomas or carcinomas also are associated with high blood pressure, together with changes in the sexual organs and secondary sexual characteristics. The mechanism of the hypertension in these cases is obscure, for there is no hyperadrenalinæmia

Pituitary Tumours. High blood pressure has been associated with the basophil adenoma of Cushing's syndrome. How far this tumour is directly responsible is doubtful; it seems likely that associated suprarenal lesions are the more important. A curious case of hypertension, hyperchromic anæmia and achlorhydria suggested overaction of the posterior part of the pituitary gland (125). Page (126) has described a *diencephalic syndrome* marked by labile hypertension, cutaneous vasomotor disturbances and lachrymation, with increase in heart rate. The basal metabolic rate is raised but partial thyroidectomy does not benefit. Women are chiefly affected. The name has been given because the symptoms are reproduced by diffuse stimulation of the diencephalon.

Pregnancy and Hypertension. Essential hypertension may occur early enough to be complicated by pregnancy, and there may have been antecedent nephritis. Apart from these types, hypertension may arise directly as a result of pregnancy. It tends to appear in the last three months. There may be albuminuria and œdema. The effective renal blood flow is normal, but the filtration rate is lowered (127). The lesion is presumably glomerular; this would account for the albuminuria: if this is profuse enough hypoproteinæmia may result, and add another cause for the œdema in addition to the salt retention. The hypertension is possibly of renal origin (128). On the termination of pregnancy the symptoms usually clear up; but in about a quarter of the cases permanent high blood pressure, similar to essential hypertension, may persist (129). If pregnancy occurs in a woman

Toxic effects are not uncommon. Fatigue, headache and vertigo and mental confusion may occur, and nausea and vomiting (141). Skin rashes, jaundice, and fatalities have been reported, even when the level in the blood has been kept under observation. Goitre occasionally develops. The toxic dose is very near the therapeutic Elderly patients may become anæmic and wasted (142) (143). When the drug is withheld the pressure rises again. Contra-indications are old age, arteriosclerosis and renal lesions. Severe and intractable headache seems to be the most important indication for its use. The symptomatic relief may surpass the fall in blood pressure (144).

In the treatment of a permanent disorder, such as hypertension, it is clear that the drug would have to be used indefinitely. It is likely that the necessity of frequent estimations of the cyanide level in the blood and the danger of toxic reaction, even with full precautions, make the remedy of little real practical value in treating hypertension in the long run.

OTHER DRUGS. Apart from the thiocyanates, the large number recommended is only an indication of their ineffectiveness. In ambulant cases (145) the effects of most preparations that have a more or less well-established reputation have been studied. None of them, under critical control, proved to be of more value than a placebo in reducing pressure. Similar observations on a number of drugs gave equally disappointing results (146). More scepticism is needed in the routine prescription of alleged hypotensive drugs, and more attention to the things that matter. Some of the sedatives gave symptomatic relief. Where nervous tension, restlessness and insomnia are a source of trouble there is a scope for the barbiturates and bromide. During an acute phase of hypertension the effect of rest is enhanced by them, and it is possible that full doses of the nitrites may help for the moment.

SPECIAL SYMPTOMS. Apart from those given above, intractable *headache* may be difficult to relieve. Venesection is sometimes effective and also lumbar puncture; intravenous magnesium sulphate, 2 grammes in a 10 per cent solution may help (22).

For *acute encephalopathy*, when œdema of the brain may be suspected, careful removal of a little cerebrospinal fluid is indicated, as well as the measures given above.

than the disease. Most important are various modifications in life and habits. If the occupation, or mode of life generally, is leading to strain and overwork and worry, suitable changes must be suggested according to the urgency of the condition. Holidays should be long and restful. Week-ends should be true days of rest, and observation of the Fourth Commandment might well be stricter. Many unnecessary activities can be cut out. Moderate exercise is beneficial, but not to cause fatigue. An extra hour in bed at night and a day in bed a week may be very beneficial. Reassurance and encouragement are essential to allay the lurking fear of some catastrophe that many of these patients secretly harbour.

DIET. If the patient is obese, reduction in weight will benefit the general health, and sometimes may be associated with reduction in pressure. *Restriction of salt is of no value. Restriction of protein* probably has little effect unless there is gross renal damage Moderation is the watchword. In a phase of severe hypertension rest in bed, on a diet of fruit and water, will reduce the pressure to a safer level for a time. Alcohol in strict moderation probably does no harm, unless there is renal damage.

TOBACCO. Nicotine undoubtedly causes vasoconstriction and a slight rise in pressure in some people (136). The effect is transient. Here, again, moderation is essential Heavy smoking, when retinal vasospasm can be detected, is certainly bad, and abstention should be enjoined.

Vitamin A given in large doses appears to be of no value (137).

Stilboestrol may give symptomatic relief in hypertension at the menopause, without conspicuous effect on the pressure

THIOCYANATE THERAPY. The thiocyanates are effective in reducing blood pressure (138). Their mode of action is unknown. The potassium salt has been used as a rule. The usual dose is 6 to 9 grains a day to begin with, and then half the dose after the first five or six days. The effective level in the blood is thus reached, which is about 10 mg per 100 cc. The level of 15 mg. per 100 cc. should not be exceeded. The level may be maintained by about 3 grains a day. About half the cases respond (140). As the rates of absorption and excretion are probably very variable, the only way to control the dosage is by frequent estimations of the thiocyanate in the blood. This may have to be done weekly at first.

Toxic effects are not uncommon. Fatigue, headache and vertigo and mental confusion may occur, and nausea and vomiting (141). Skin rashes, jaundice, and fatalities have been reported, even when the level in the blood has been kept under observation. Goitre occasionally develops. The toxic dose is very near the therapeutic. Elderly patients may become anæmic and wasted (142) (143). When the drug is withheld the pressure rises again. Contra-indications are old age, arteriosclerosis and renal lesions. Severe and intractable headache seems to be the most important indication for its use. The symptomatic relief may surpass the fall in blood pressure (144).

In the treatment of a permanent disorder, such as hypertension, it is clear that the drug would have to be used indefinitely. It is likely that the necessity of frequent estimations of the cyanide level in the blood and the danger of toxic reaction, even with full precautions, make the remedy of little real *practical value* in treating hypertension in the long run.

OTHER DRUGS. Apart from the thiocyanates, the large number recommended is only an indication of their ineffectiveness. In ambulant cases (145) the effects of most preparations that have a more or less well-established reputation have been studied. None of them, under critical control, proved to be of more value than a placebo in reducing pressure. Similar observations on a number of drugs gave equally disappointing results (146). More scepticism is needed in the routine prescription of alleged hypotensive drugs, and more attention to the things that matter. Some of the sedatives gave symptomatic relief. Where nervous tension, restlessness and insomnia are a source of trouble there is a scope for the barbiturates and bromide. During an acute phase of hypertension the effect of *rest* is enhanced by them, and it is possible that full doses of the nitrites may help for the moment.

SPECIAL SYMPTOMS. Apart from those given above, intractable *headache* may be difficult to relieve. Venesection is sometimes effective and also lumbar puncture; intravenous magnesium sulphate, 2 grammes in a 10 per cent solution may help (22).

For *acute encephalopathy*, when œdema of the brain may be suspected, careful removal of a little cerebrospinal fluid is indicated, as well as the measures given above.

than the disease. Most important are various modifications in life and habits. If the occupation, or mode of life generally, is leading to strain and overwork and worry, suitable changes must be suggested according to the urgency of the condition. Holidays should be long and restful. Week-ends should be true days of rest, and observation of the Fourth Commandment might well be stricter. Many unnecessary activities can be cut out. Moderate exercise is beneficial, but not to cause fatigue. An extra hour in bed at night and a day in bed a week may be very beneficial Reassurance and encouragement are essential to allay the lurking fear of some catastrophe that many of these patients secretly harbour.

Diet. If the patient is obese, reduction in weight will benefit the general health, and sometimes may be associated with reduction in pressure. Restriction of salt is of no value. Restriction of protein probably has little effect unless there is gross renal damage. Moderation is the watchword. In a phase of severe hypertension rest in bed, on a diet of fruit and water, will reduce the pressure to a safer level for a time. Alcohol in strict moderation probably does no harm, unless there is renal damage.

Tobacco. Nicotine undoubtedly causes vasoconstriction and a slight rise in pressure in some people (136). The effect is transient. Here, again, moderation is essential. Heavy smoking, when retinal vasospasm can be detected, is certainly bad, and abstention should be enjoined.

Vitamin A given in large doses appears to be of no value (137)

Stilboestrol may give symptomatic relief in hypertension at the menopause, without conspicuous effect on the pressure

Thiocyanate Therapy. The thiocyanates are effective in reducing blood pressure (138). Their mode of action is unknown. The potassium salt has been used as a rule. The usual dose is 6 to 9 grains a day to begin with, and then half the dose after the first five or six days. The effective level in the blood is thus reached, which is about 10 mg. per 100 cc. The level of 15 mg. per 100 cc. should not be exceeded. The level may be maintained by about 3 grains a day. About half the cases respond (140). As the rates of absorption and excretion are probably very variable, the only way to control the dosage is by frequent estimations of the thiocyanate in the blood. This may have to be done weekly at first.

... and surgical results
... oubt, the really
(15.) ... result was that the cases with the ... retinal changes
... than those
... rvived five
years as against 31 per cent treated ... Allen and Adson (155), the bulk of whose cases, graded by ocular changes, were type 3, with definite retinopathy, found that in about one-third the pressure fell. In another series reported on this type of case it must be noted that the surgical results were discouraging (156) The results of the more extensive sympathectomy practised by the supradiaphragmatic route have been reported. Four hundred and thirty-seven cases have been followed for five to ... years. There was complete relief from severe symptoms in

... was notable, and there was significant decrease in the size of the heart in about one half. After five to seven years nearly sixty per cent were alive; about four-fifths of these patients were regarded as having progressed to serious disease (157. Smithwick (158) has reported on a smaller series of one hundred and fifty-six patients, using different grouping, based on the pulse pressure. The results were gauged on the reading of the diastolic pressure at rest. About one-third of the patients watched for over one to five years were certainly improved.

Selection of Cases. There seems to be general agreement that patients over fifty years of age, and anyone who has had heart failure or a stroke, should be excluded. Renal damage severe enough to cause nitrogen retention, should also exclude. Perhaps the rate at which the renal deficiency has developed is the important point The quicker the rate the graver the significance. Some think papillœdema unfavourable, but on this point the reports are discordant. Operation might be the one chance. Obesity will be unfavourable, and also emphysema or alcoholism. A labile pressure responds better than a fixed one. For this purpose the effects of sodium amytal (3 grains every hour for three hours) are observed, and also the effects of change in posture. A fall in the diastolic pressure to 110 augurs well (159).

Intractable headache and other such cerebral symptoms indicate

TISSUE EXTRACTS. Renal extracts are still in the experimental stage. Theoretically and on experimental grounds, there is reason to suppose that the normal kidney produces an antipressor substance, hypertensinase (147). Page (148) has reported encouraging results. Others have not confirmed them (149). The pyrogenic effect of these substances makes evaluation difficult, and there are also anaphylactoid effects. There is enough experimental evidence to provide hope for the future. If some effective neutralising substance can be found, its administration may control hypertension, although it may not cure; much as does insulin or liver extract (150).

Surgical Treatment. SPLANCHNICECTOMY. The aim is to bring about a lowering of the blood pressure by removing the vasomotor control from as much of the splanchnic area as possible and to promote more stable and more profuse supply to the kidneys. Various operations have been devised, differing mainly in their extent. Those with the more limited range are confined to the subdiaphragmatic area. Those more extensive are supradiaphragmatic as well. Owing to technical difficulties the assessment of result is not easy, nor is it easy to gauge the effectiveness of surgical procedures in a disease which runs so long a course and may be met with in such varying stages as essential hypertension. It is possible now to consider the results in several series.

The most extensive surgical procedure is that elaborated by R. H. Smithwick (151), who removes by lumbodorsal splanchnicectomy all the sympathetic chain, first on one side and then on the other, between the eighth dorsal and the first lumbar ganglia. The roots of the great splanchnic nerve from the 6, 7, 8 dorsal ganglia are cut and also its peripheral connections. The same applies to the lesser and least splanchnic nerves. Peet and Woods (152) also operate above the diaphragm. Allen and Adson (153) keep below it. It would appear that Smithwick's lumbodorsal technique is likely to be the choice in future.

RESULTS. It must be remembered that splanchnicectomy does not cure the disease, for it cannot remove the cause; but it can prolong life and relieve symptoms. The criteria of success are variable. Some stress the changes in blood pressure, some the increase in longevity, and others the symptomatic improvement. This makes the various series difficult to compare.

no cure, it does offer some possibility of the relief of symptoms, even of the grave ocular type. There is probably some increase in longevity in early cases, but here the long natural course of the disease still exceeds the time so far available for the evaluation of this point. A survey of cases after twenty years will, no doubt, be valuable. But by then perhaps some humoral method of cure will be available.

The literature on this subject is now very large. For a full and clear survey the reader is recommended to turn to "An Introduction to Essential Hypertension," by R. F. Herndon (1946, C. Thomas, Illinois). The monographs by Goldring and Chasis, and Page and Corcoran to which reference has been extensively made, are full of valuable first-hand information.

REFERENCES

1 Page, Corcoran (1945). "Arterial Hypertension" Chicago.
2 Wiggers (1945) "Physiology in Health and Disease" Philadelphia
3 (1939) *Amer Heart J*, 18 95
4 (1939) *J Amer med Assoc*, 113, 291
5 Rappoport, Linsada (1944) *J Lab. and clin Med*, 29, 635
6 Steele (1942) *J Mt Sinai Hosp*, 8, 1042
7 Gambill Hines (1944) *Amer Heart J* 28, 763
8 Kolte *et al* (1944) *Amer Heart J*, 28, 780
9 Wendkos Rosman (1943) *Amer Heart J*, 26 623
10 Gambill, Hines (1944) *Amer. Heart J* 28, 777
11 Alam, Smirk (1943) *Brit Heart J*, 5 152
12 Stewart, Haskell, Brown (1945) *Amer Heart J*, 30, 541
13 Hines (1940) *J Amer med Assoc*, 115, 271
14 Alam, Smirk (1943) *Brit Heart J*, 5, 156
15 Smirk (1944) *ibid*, 6, 176
16 Levy *et al* (1945) *J Amer med Assoc* 128, 1059
17 Hines, Brown (1933) *Ann intern Med*, 7 209
18 Russell (1943) *Amer Heart J*, 26, 398
19 Russek Zohman (1945) *Amer Heart J*, 29, 113
20 Feldt Weinstrand (1942) *Amer Heart J*, 23, 766.
21 Pickering, Kissin (1936) *Clin Sci* 2 201
22 Goldring, Chasis (1944) "Hypertension" New York
23 Miller Bruger (1939) *Amer Heart J*, 18, 329
24 Alam Smirk (1938) *Clin Sci*, 3, 259
25 Hines (1940) *Amer Heart J* 19, 408
26 Garai (1945) *Brit Heart J* 7, 200
27 Kesilman (1941) *Med Record*, 154, 16.
28 Weis Prosmark (1938) *Amer J med Sci*, 195, 510
29 Master, Marks Dacks (1943) *J Amer med. Assoc* 121, 1251
30 Aymar (1934) *Arch intern Med*, 53, 792
30a Platt (1947) *Quart J Med*, 16 111
31 Wood Cash (1939) *Ann intern Med*, 13, 81
32 Robinson, Bruger (1940) *Arch intern Med*, 66, 393
32a East (1947) *Practitioner*, 158, 487
33 Miller (1934) *J Inst Actuaries*, 65, 353
34 Parkinson, Hoyle (1934) *Lancet*, 2 913
35 Bisgard (1939) *Arch intern Med*, 63, 497.

operation. Biopsy of the pectoral muscle may give some guide to the extent of arteriolar sclerosis. The ratio of the thickness of the wall to the lumen of the vessel is noted. The evidence is only local however (160).

Effects of Sympathectomy on the Circulation. Postural hypotension will probably occur if the operation has been sufficiently extensive. In some respects this resembles the natural or idiopathic orthostatic hypotension. But there is this difference; the pulse in idiopathic hypotension does not accelerate on assuming the erect posture. After sympathectomy the pulse is faster, lying and standing. On raising the patient to 60°, the systolic pressure tends to fall twice as much, and the diastolic seven times as much, as before operation. The response to the Flack test (forced expiration against the pressure of a column of mercury) is greatly impaired, for the blood pressure falls severely. The output of the heart increases, but the stroke volume is less when the head is up, as might be expected from the lowered venous return (161).

Sleeping with the head of the bed raised, and the use of an abdominal binder helps to mitigate the symptoms of postsympathectomy hypotension (162). Paredrinol sulphate (10-20 mg. subcutaneously) may be tried.

The patient must be warned that for a time he may feel faint and giddy on standing up, and that it is a good sign. By some mechanism, at present not understood, patients gradually recover from this postural hypotension. As the last authors suggest, *possibly those who develop it are those in whom the neurogenic* influences predominate; more information is needed about these cases.

How far renal function may be improved is doubtful. Goldring and Chasis (22) observed no increase in the renal blood flow after operation. Impotence may result from excision of the second lumbar ganglion, but this may only be temporary. There will be sterility. On the whole mortality is low; but the clinical results are difficult to predict. A neurotic patient is less likely to prove a success than one with more stable mentality. Even if there be considerable fall in the blood pressure after operation at first, it may have resumed its original level after a year or eighteen months.

Conclusion. Although the operation of splanchnicectomy is

no cure, it does offer some possibility of the relief of symptoms, even of the grave ocular type. There is probably some increase in longevity in early cases, but here the long natural course of the disease still exceeds the time so far available for the evaluation of this point. A survey of cases after twenty years will, no doubt, be valuable. But by then perhaps some humoral method of cure will be available.

The literature on this subject is now very large. For a full and clear survey the reader is recommended to turn to "An Introduction to Essential Hypertension," by R. F. Herndon (1946, C. Thomas, Illinois). The monographs by Goldring and Chasis, and Page and Corcoran to which reference has been extensively made, are full of valuable first-hand information.

REFERENCES

1 PAGE, CORCORAN (1945) "Arterial Hypertension" Chicago
2 WIGGERS (1945) "Physiology in Health and Disease" Philadelphia
3 (1939) *Amer Heart J* 18 93
4 (1939) *J Amer med Assoc*, 113, 294
5 [illegible]
6 [illegible] *Med*, 29 638
7 [illegible]
8 [illegible] 763
9 [illegible]
10 [illegible] 26 623
11 [illegible] 777
12 [illegible]
13 [illegible] *Heart J*, 30 341
14 [illegible]
15 [illegible] 6, 178
16 LEVY, *et al* (1945) *J Amer med Assoc* 128 1059
17 HINES BROWN (1933) *Ann intern Med* 7, 209
18 RUSSELL (1943) *Amer Heart J* 26, 398
19 RUSSEK ZOHMAN (1945) *Amer Heart J* 29 113
20 FELDT, WEINSTRAND (1942) *Amer Heart J* 23 766
21 PICKERING KISSIN (1936) *Clin Sci* 2 201
22 GOLDRING CHASIS (1944) "Hypertension" New York
23 MILLER BRUGER (1939) *Amer Heart J* 18 329
24 ALAM SMIRK (1938) *Clin Sci*, 3, 259
25 HINES (1940) *Amer Heart J* 19, 408
26 GARAI (1945) *Brit Heart J* 7 200
27 KESILMAN (1941) *Med Record*, 154 16
28 WEIS, PROSMARK (1938) *Amer J med Sci* 195 510
29 MASTER, MARKS, DACKS (1943) *J Amer med Assoc* 121 1251
30 AYMAR (1934) *Arch intern Med* 53, 792
30a PLATT (1947) *Quart J Med*, 16, 111
31 WOOD CASH (1939) *Ann intern Med* 13, 81
32 ROBINSON BRUGER (1940) *Arch intern Med*, 66 393
32a EAST (1947) *Practitioner* 158 467
33 MILLER (1934) *J Inst Actuaries* 65 353
34 PARKINSON, HOYLE (1934) *Lancet*, 2 913
35 BISGARD (1939) *Arch intern Med* 63, 497

36 MOUNTAIN, *et al* (1943) *Amer. Heart J.*, **26**, 528
37. GOLDBLATT, *et al* (1934) *J exper. Med*, **59**, 347.
38 PAGE (1939) *Science*, **89**, 273
39 PAGE (1935) *Amer J. Physiol*, **112**, 166
40. GOLDBLATT, *et al* (1937) *J. exper Med*, **65**, 233
41 GLENN, CHILD, PAGE (1938) *Amer J. Physiol*, **122**, 506.
42 FREEMAN, PAGE (1937) *Amer Heart J*, **14**, 405
43 GOLDBLATT (1937) *Ann intern Med*, **11**, 69
44 BOUCKAERT, *et al* (1939). *J Physiol*, **96**, 44
45 FASCIOLO, *et al* (1938) *J Physiol*, **94**, 281.
46. PAGE (1940) *J exper Med*, **72**, 301
47 PAGE (1940) *Amer J Physiol*, **130**, 22
48. LEWIS, GOLDBLATT (1942) *Bull New York Acad Med.*, **18**, 459
49 SWINGLE, *et al* (1939) *Amer J Physiol*, **127**, 768
50. GOORMATIGH (1939) *Brux Med*, **15**, ii, 1541
51 RUDBARD (1941) *Amer J Physiol*, **135**, 124
52. [illegible]
53
54 [illegible] 283
55. [illegible]
56 [illegible]
57. PAGE (1941) *Amer J Physiol*, **134**, 789
58 WILKINS, DUNCAN (1941) *J. clin Invest*, **20** 721
59 BRADLEY, PARKER (1941) *J clin Invest*, **20**, 715
60 LORBER (1942) *Amer Heart J* **23**, 1.
61 CORCORAN, PAGE (1940) *Amer J Physiol*, **130**, 335
62 CORCORAN, KOHLSTAEDT, PAGE (1941) *Proc Soc Exper Biol and Me*[illegible] **46**, 244
63. GOLDRING *et al* (1941) *J clin Invest*, **20**, 637
64 QUMIBY, *et al* (1945) *J clin Ivest*, **24**, 69
65 GREGORY, *et al* (1945) *Arch intern Med*, **76**, 11
66 CORCORAN, PAGE (1941) *J Amer med Ass*, **116**, 690
67 BLALOCK, LEVY (1937) *Ann Surg*, **106**, 826
68 DEXTER, BRAUN-MENENDEZ (1941) *Rev Soc argent de Biol*, **17**, 3[illegible]
69 RODBARD, KATZ (1941) *J exper Med*, **73**, 357
70 BRAUN-MENENDEZ, *et al* (1940) *Amer J med Sci*, **200**, 608
71 HAYNES, DEXTER (1945) *J clin Invest*, **24**, 75
72 CORCORAN, PAGE (1942) *Amer J Physiol*, **135**, 361
73 PAGE (1941) *J Mt Sinai Hosp*, **8**, 3
73a TRUETA, BARCLAY, FRANKLIN, *et al* (1947) "Studies of the Renal C[illegible] culation," Oxford
74. PICKERING (1943) *Brit med J*, **2**, 1
75 HAMILTON, COLLINS (1942) *Amer J Physiol*, **136**, 275
76 BLACKMAN (1939) *Johns Hopkins Hosp Bull*, **65**, 353
77 SAPHIR, BALLINGER (1940) *Arch intern Med*, **66**, 541
[illegible] (1939) *Trans Assoc Amer Phys*, **54**, 69
[illegible] *ed Sci*, **199**, 601
[illegible] *Acad Med*, **19** 449
[illegible] *d*, **73**, 123
[illegible] 19
[illegible] **7**, 139.
[illegible] *d*, **16**, 143
[illegible] **19**, 25
[illegible]
[illegible] *ern Med*, **60**, 772
[illegible] **21**, 539
[illegible] *Invest*, **15**, 63

90 WIGGERS (1942) *Bull, New York Acad Med*, 18, 3
91 STEELE (1937) *Amer Heart J*, 14, 452
92 WILLIAMS, LENNOX (1939) *Quart J Med*, 8, 185
93 FISHBERG (1939) "Hypertension and Nephritis," 4th ed
94 ODELL (1940) *Arch intern Med*, 66, 579
95 WILSON BYROM (1941) *Quart J Med*, 10 65
(1940) *Amer Heart J*, 19, 182
160.
19 199
med Ass, 121, 1256
117
atterns" Baltimore
203, 634
140.
105 SCHNUR (1941) ...
106 ROESTER, *et al* (1940) *Ann. intern Med*, 13, 1814
107 RUSSEK, ZOHMAN (1945) *Amer Heart J.*, 30, 427.
107a EAST, BAIN (1949) *Brit. Heart J* (in the press)
108 PICKERING (1934) *Clin Sci*, 1, 397
109 EDMONDSON, HOXIE (1942) *Amer Heart J*, 24, 719
110 PICKERING (1939) *Brit med J* 1 1
111 HORNS (1944) *Amer Heart J*, 28 435
112 MCGEORGE (1945) *Quart J Med*, 14 171
113 ELLIS (1942) *Lancet* 1, 1
114 PAGE (1939) *Ann intern Med*, 12, 978
115 ELLIS (1938) *Lancet*, 1, 977
116 GOLDBLATT, *et al* (1943) *J exper Med* 77, 297
117 GRIFFITH LINDMAN (1944) *Amer Heart J*, 28, 758.
118 STEELE (1941) *J clin Invest*, 20 473
119 FRIEDMAN, *et al* (1941) *J clin Invest*, 20, 107.
120 STROMBEK HEDBERG (1939) *Acta Chir Scand*, 82, 177
121 HOWARD, BARKER (1937) *Johns Hopkins Hosp Bull*, 61, 371.
122 BINGER, CRAIG (1938) *Proc Staff Meet Mayo Clin*, 13, 17
123 EVANS, STEWART (1942) *Amer Heart J*, 24, 835
124 MACKEITH (1944) *Brit Heart J* 6, 1
125 JONES (1938) *Lancet* 1 11
126 PAGE (1935) *Amer J med Sci*, 190, 9
Invest 21, 63
201, 395
039
Invest, 23, 742
3, 353
21, 747
765
38
9
62
11 710
411
9 736
12, 1120
40
18
1, 109

147. WAKERLIN, *et al* (1943) *Amer Heart J.*, **25**, 1
148. PAGE, *et al.* (1943) *Ann intern Med*, **18**, 29.
149 SCHATZ, *et al* (1942) *Amer J. med Sci*, **204**, 797
150 GOLDBLATT, *et al* (1942) *J Amer med Ass.*, **119**, 1192.
151 SMITHWICK (1940) *Surgery*, **1**, 1.
152. PEE- [illegible] s, **115**, 1785
153 ALL [illegible] 0
154 WO [illegible] 08
155 ALL [illegible]
156 DE [illegible] *d Ass*, **118**, 501
157 PEE [illegible] 1
158 SMITHWICK (1944) *Ann Surg*, **49**, 180
159 ADSON, ALLEN (1937) *Proc Staff Meet Mayo Clin*, **12**, 75
160 FOA, *et al* (1943) *J clin Invest*, **22**, 727
161. GAMBILL, *et al.* (1944) *Amer Heart J*, **27**, 360
162. GAMBILL, *et al.* (1944) *Amer Heart J.*, **27**, 381

CHAPTER V

DISORDERS OF THE PULMONARY CIRCULATION

Much interest has developed during recent years in various conditions which arise in the pulmonary circulation and affect the right side of the heart. The general acceptance of right ventricular failure, originally suggested by James Hope a century ago, has given importance to the lesser circulation. It is worth while recalling that Servetus in the sixteenth century, and three centuries before him, the Arabian physician Ibn-an-Nafir, had a clear idea that the blood circulated through the lungs, as R. A. Young pointed out in the Harveian Oration in 1929. There are a number of pathological conditions in the lungs which cause embarrassment of the right ventricle, some confusion in nomenclature exists at the moment owing to the widespread use of the somewhat colloquial expression which hardly merits the dignity of a Latin designation "Cor pulmonale." Now that it is appearing in acute, subacute, and chronic forms, one would suggest that it were dropped, and a more precise diagnosis attempted. The same applies to the name "Ayerza's Disease." What it was that caused the "cardiacos negros" to die of right ventricular failure was never very clear, the substitution of the word "syndrome" leads to still greater obscurity, and in the interests of accuracy it would be well to drop this expression too.

The opportunities afforded by radiology, by the electrocardiograph, and by estimations of the rate of the circulation through the lungs, have opened up a rapidly expanding field of investigation. But the impossibility of estimating directly the pulmonary arterial and venous pressures has left a serious gap, such as would be felt if there were no means of measuring the arterial and ven[illegible]

[illegible] the pressures in that chamber, and so indirectly of those in the pulmonary artery.

In this chapter we will consider:

1. Lesions of the pulmonary arteries.
2. Pulmonary embolism and infarction.
3. Pulmonary disease.
4. Deformities of the chest.

All these may be associated with primary right ventricular failure. Secondary right ventricular failure, which follows failure of the left ventricle, and which is indeed much the commonest cause of enlargement and failure of the right ventricle, (2) is discussed in another chapter. The two are merely distinguished for convenience from the point of view of causation, not because there is any essential difference in their hæmodynamics. But it is worth recalling that some of these conditions produce examples, pure and uncomplicated, of the symptoms of failure of the right ventricle in a way which is relatively rare (2); in others the symptomatology is confused by pulmonary lesions, much as in those cases where the pulmonary circulation is primarily affected by failure of the left ventricle.

Valvular disease of the right side of the heart is rare on the whole; and the right ventricle escapes the ischæmic changes due to coronary sclerosis. In nearly all the pathological conditions now under discussion the failure of the right ventricle is brought about by the overload caused by raised pressure due to obliteration of the circulatory bed.

Direct measurement of the pressure in the pulmonary artery at operation gave a figure of about 30 mm. Hg. (1). Recently it has been possible to measure the pressure in the right ventricle by means of the cardiac catheter. In normal patients the systolic pressure varied from 18 to 30 mm. Hg, with an average of 25 mm. Hg. In cases of pulmonary fibrosis and emphysema, when failure was not present, the pressures were normal in five cases; in twelve others the pressures at systole ranged from 35 to 58 mm. Hg., the pulse pressure being from 30 to 54 mm. Hg. (24).

Lesions of the Pulmonary Arteries

The pulmonary arterial system has to withstand a lower pressure than the systemic, so its structure is modified accordingly. The walls

of the pulmonary artery are thinner and the coats of the smallest arterioles down to 0.1 mm. in diameter are less muscular (2)

Atheroma. It may be because there is less hydraulic wear and tear than in the systemic circulation that the degenerative lesions, such as atheroma, are less conspicuous. Nevertheless, some form of sclerosis of the pulmonary arteries is generally found at autopsy on elderly patients, and the older the patient the more conspicuous are the lesions (4). A time factor is therefore apparent. The other factor, an abnormal pressure, can also be inferred. Atheromatous deposits in the main stem and larger branches are usually more pronounced in patients who have had some form of chronic pulmonary disease (5) such as fibrosis or emphysema (6); or mitral stenosis for many years (7) There is almost invariably some dilatation of the pulmonary artery when much atheroma is present, suggesting some stretching either from loss of elasticity, or due to increase of pressure, or to both together. The atheromatous deposits rarely reach the degree of severity of those in the aorta Ulceration and calcification is rare (4). Pulmonary atherosclerosis by itself plays little or no part in causing embarrassment to the right ventricle (8) The atheromatous areas may provide sites favourable for the formation of thrombi (7). Their importance may lie in pointing to an increase in pulmonary pressure. Their incidence is in no way parallel to the amount of atheroma in the systematic arterial circulation

Arteriolar Lesions. *Subintimal thickening and hypertrophy* of the middle coats of the smaller arteries and arterioles is also found. These changes have been noted in mitral stenosis and are presumably the result of increased pressure due to chronic engorgement (7). The arteriolar bed may be extensively affected in this way in cases with emphysema (5). They were more or less parallel in severity with the degree of emphysema. One may suppose that here the changes were the result of increased pressure resulting from obliteration of the capillary bed by the emphysema. Atheroma of the larger branches is often pronounced in these cases (10). Similar lesions may be found in lungs which have been the seat of fibrotic disease, sometimes tuberculous in character. These are examples of what have been termed secondary sclerotic arterial lesions (2). If severe enough they tend to overload the right ventricle.

Syphilitic Endarteritis. Syphilis of the lungs is very rare The characteristic lesion is widespread endarteritis obliterans of the pulmonary arterioles. The main artery and its branches may show the characteristic lesions of syphilis similar to those found in the aorta. *The trunk is usually dilated and there is also extensive* atheromatous degeneration (11, 12). The obstruction in the arteriolar bed appears to be largely responsible for the dilatation and degeneration of the larger branches and main trunk (13). There is nodular fibrosis scattered throughout the lungs as well as the arteriolar lesions, in which the latter become involved. This disease becomes manifest in middle life and causes progressive failure of the right ventricle. Congenital syphilis may cause it.

Pulmonary Schistosomiasis. Infection of the lungs by bilharzia, schistosoma hæmatobium, may lead to widespread endarteritis. The vessels are obliterated, recanalised, and are *surrounded by angiomatoid new tissue. There is medial hypertrophy.* These obliterative changes cause a rise in pressure and *gross dilatation of the pulmonary artery*, with *atheromatous* degeneration, and incompetence of its valves. The right ventricle becomes grossly enlarged and fails. *When the right ventricle fails* to overcome the resistance, cyanosis develops. There are no parenchymatous lesions of the lungs. The disease is not uncommon in Egypt (14, 15).

Pulmonary Hypertension and Idiopathic or Primary Pulmonary Arteriosclerosis. In this group there are three conspicuous features. The first is progressive and intractable *failure of the right ventricle.* This is marked by the characteristics given elsewhere. The patients are often young, but may be old. There is usually cyanosis, which may be severe. There are the usual findings of œdema, hepatic and jugular engorgement, and ascites. Dyspnœa is slight and orthopnœa absent. The rhythm is regular.

2. The *right ventricle* is greatly enlarged, with right axis deviation in the cardiogram, and at autopsy shows hypertrophy. (Plate 20.) The *pulmonary artery is dilated in the skiagram* and at autopsy, and clinically the loud second sound indicates high pressure within it. *The dilatation may lead to incompetence of* the pulmonary valves (16).

3. The *pulmonary arterioles* show a *somewhat variable picture.*



PLATE 20

Pulmonary Hypertension.

Antero-posterior and right anterior oblique views.

(*Brit. Heart Jnl.*)

ere may be only local changes with tendency to thrombus mation (17) There may be a tendency to hypertrophy of the uscular coats with a proliferation of the elastica and intima (18) 0). On the other hand, the arteriolar hypertrophy and obliteraon may be only slight, although atheromatous deposits may be und down to the quite small branches Finally there may be no icroscopical changes in the pulmonary arteries of an obliterative ture and even the medial hypertrophy may be inconspicuous 0, 21, 22).

The clinical and post-mortem findings, of which the outstanding ature is the failure, in the end often rapid, of an hypertrophied ght ventricle, need explanation, Syphilitic endarteritis, and arenchymatous pulmonary disease, except in one case where there as curious disintegration of the lung tissue which may have been erminal (19) can be excluded. The changes in the pulmonary rtery and the main branches are those of dilatation and atheroatous degeneration, such as are found when in all probability, he pressure in it is high. If one can trace a progressive sequence f arteriolar change from little or none to moderate and patchy nedial hypertrophy and intimal proliferation, it is evident that hey are not the cause of the events behind them, but more likely o be the result of the, at present, unidentified cause. If one allows or minor anatomical differences in the structure of the pulmonary arteries, such changes as are found, excluding atheroma, are not unlike those resulting from arterial hypertension in the systemic circulation, even to some degrees of necrosis (19). It may be recalled that for many years there was doubt as to whether *these* were not the cause of the raised pressure. and indeed until the sphygmomanometer was introduced their nature was not appreciated at all. By analogy, although it cannot be proved without measuring the pressure in the pulmonary circulation, it is possible that a state of primary or essential pulmonary ... which ... nd the ... the right ventricle, and leads to its ultimate failure (22, 19, 21). The converse suggestion, that the dilatation is congenital and the obliterative process compensatory (23), appears to be quite unlikely

Observations of the pressure in the right ventricle will ...

valuable information in these cases, and some indication of what the accuracy of the inference may be as to the pressure in the pulmonary artery.

REFERENCES

1. Brock (1941). *Guy's Hosp Rep.*, 90, 217.
2. Brenner (1935) *Arch intern. Med*, 56, 217.
3 Thompson, White (1936) *Amer Heart J*, 12, 641.
4. Brenner (1935) *Arch intern Med*, 56, 457
5. [illegible]
6
7
8.
9
10
11.
12.
13
14. Shaw, Ghareeb (1938). *J Path Bact*, 46, 401
15. Bedford, Aidans, Gorgis (1946) *Brit Heart J*, 8, 87.
16 McGuise, McNamara (1937) *Amer Heart J*, 14, 562
17 Staemmler (1938) *Arch f Kreislaufforsch*, 3, 125
18 Darley, Doan (1936) *Amer J med Sci*, 191, 633
19 Barrett, Cole (1946) *Brit. Heart J*, 8, 76
20 [illegible] *Brit Heart J*, 2, 177
21
22.
23
24 25, 639

Pulmonary Embolism and Infarction

The tragic event of sudden death, some ten days after an operation, due to a large clot lodged in the pulmonary artery has long been familiar enough. Since the paper of McGinn and White (1), which pointed out that certain changes in the cardiogram might follow pulmonary infarction, much interest has been roused in the pathogenesis of these curves, and also in the clinical diagnosis of pulmonary embolism and infarction, and their effects on the right ventricle. Owing to the coincidence of several variable causes there is still a good deal of obscurity on a number of points.

Clinical Features. A large embolus causes death in a few seconds. The patient cries out, complains of precordial pain and suffocation, and in a few moments all is over. At autopsy the pulmonary artery is found to be blocked by a long grey clot coiled up at the bifurcation, and the chambers of the right side are greatly dilated. Smaller emboli passing into the lungs cause infarcts which vary in size according to the size of the branch of the

pulmonary tree in which they may lodge We have noted that the larger emboli are apt to be found in surgical cases, and the smaller, with infarcts, in medical.

Symptoms. These vary a great deal. RESPIRATORY. There is usually dyspnœa and a sense of suffocation. The rate of breathing increases (tachypnœa) and the breaths may become deeper (hyperpnœa). Large to moderate-sized pulmonary emboli in dogs caused increase in rate and depth of respiration. Tachypnœa alone resulted from emboli in the smallest arterioles (2). These respiratory changes are of reflex origin arising from stimuli in the lungs, and are abolished by vagotomy. Later there may be pain from pleurisy over the infarct, cough, and sometimes hæmoptysis. There may be dullness, and altered breath sounds, distant or bronchial, and friction rubs may be heard. An effusion, often hæmorrhagic, may form in the pleural sac.

CARDIAC. There may be substernal oppression, or even severe pain, but it is localized, and not inclined to radiate as in coronary occlusion. The onset is very sudden, "like a blow." The rate of the heart increases; occasionally an abnormal rhythm results, such as fibrillation The pulmonary second sound is increased in loudness. Over the right ventricle a gallop rhythm may be heard. Engorgement of the jugular veins is probably common but often quite transient (3). Enlargement of the right ventricle and auricle is shown in the skiagram. Cyanosis is apt to develop. Experimentally, cyanosis is more likely to arise from emboli in terminal arterioles, and is associated with dyspnœa. Embolism of the larger trunks causes pallor and syncope (4). If the emboli are large, experiments show that the right ventricle dilates, and the venous pressure rises, the effect being purely mechanical (5).

PERIPHERAL. In about one-third of cases shock predominates (6). The skin is cold and perspiration is profuse. The blood pressure falls and the aspect shows greyish pallor. The patient feels great fear (1) and is faint and may lose consciousness. Later there may be fever, and slight jaundice from absorption of pigment from the infarct.

A Complication of Heart Disease. These clinical symptoms may be recognised easily when they arise in patients after operation. But pulmonary infarction also occurs frequently in patients with heart failure ; then th...

tion may be less acute (3). The patient's progress may be checked; and a sudden step downwards may be noted. The complication *may hinder improvement and prove a "last straw" to an over*-burdened heart. The symptoms may be mild and the lesion latent. Fever, tachycardia and sudden deterioration are the usual indications. We believe that the extensive thrombosis of the pulmonary arteries sometimes found at autopsy in patients who have been slowly dying of heart failure may cause a similar final breakdown. Embolism is not the cause here; the extent of the thrombosis and infarction may be very extensive, and may be the final cause of death (7).

Radiological Findings. Here, there is much variation Small infarcts may cast no shadow. There may be embolic obstruction without infarction. The variation in size and shape of the infarcts when present, and the changes which occur in them in the course of time make accurate *diagnosis difficult. Some shadows are* triangular, later they tend to become linear Sometimes they are

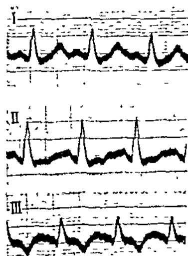


FIG. 25A
Pulmonary infarction First day. Note S_1, and negative T_2 and T_3

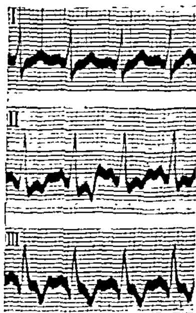


FIG 25B
Pulmonary *infarction* Third day From the same case as 25A, showing further changes

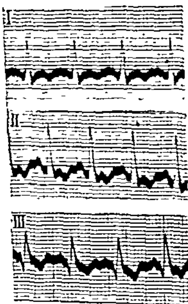


FIG 25c
Pulmonary infarction Fifth day
Regression

circular like an abscess cavity. Others resemble the shadows of pneumonia. There are also the additional complications of shadows due to collapse, elevation of the diaphragm, and perhaps a pleural effusion (8) But in cases of doubt a skiagram with a portable apparatus is always worth taking; the diagnosis of infarction must be considered with the other possible causes

Cardiographic Changes. LIMB LEADS. Since the paper of McGinn and White (1) these have aroused much interest, and speculation as to their ætiology. The problem is by no means solved. These observers described the appearances of an S wave in lead I, with a negative S-T phase. The same S-T negativity was apparent in lead II Lead III showed a Q wave, and later a negative T wave They emphasised the transient character of these changes which might only last forty-eight hours. Later writers (9) have confirmed the presence of these changes in many cases, but on the whole they are not frequent and normal curves may be found. On the other hand coexisting myocardial disease, such as coronary sclerosis and hypertension, is so common in these cases, that the effects of this complication in the curve must be an important cause of anomalous records. Another point is the very transient duration of the changes, which may last a few hours only (Fig. 25 A, B, C).

CHEST LEADS. Negative T-waves may occur in CR_1, CR_2, CR_3. Since T is always upright in these leads *in health*, the changes are of diagnostic importance, the T in CR_1 remaining negative longest (10). The curve returns to normal after any period up to eight

weeks (3). Similar changes have been noted in lead CF_2 (9); but they are only significant if a tracing prior to the embolus has been normal, since a vertical position of the heart may cause T to be negative in this lead.

DIFFERENTIAL DIAGNOSIS IN CARDIOGRAMS. The curves in the limb leads bear a superficial resemblance to those of posterior infarction. But in pulmonary embolism Q-waves do not occur in lead II, nor is the ST junction elevated; also an S in lead I is not part of the pattern of posterior infarction, and T is not inverted in the chest leads. They resemble more closely the pattern of right ventricular hypertrophy, with an S in lead I, R greater than S in CR_1, and inverted T-waves in CR_1, CR_2, and CR_3. Somewhat similar curves have been found in pneumonia, and the cause of each is probably right ventricular stress (3). The progressive evolution of changes characteristic of the curves of infarction is not seen (11).

CAUSES OF THE CURVES OF PULMONARY EMBOLISM AND INFARCTION. First of all it must be noted that the effects on the right ventricle of pulmonary embolism and infarction are very varied. Pulmonary embolism may cause no embarrassment at all, or a very small infarct may be associated with the development of serious deficiency. There are the following possibilities to be considered (6):

1. The effects of mechanical strain, caused either by the embolic obstruction, or reflex spasm in the pulmonary bed.
2. Reflex spasm in the right coronary artery following the pulmonary lesion (12).
3. The effects of shock on the coronary circulation, which may or may not be the seat of disease.
4. The effects of anoxæmia on the myocardium.
5. Engorgement of the right auricle may cause obstruction to the venous drainage from the coronary vein (13, 9).

1. *Mechanical Strain.* Ligation of a main pulmonary artery for pulmonectomy produced right axis deviation, with the appearance of an S-wave, and depression of S-T in lead II. These changes lasted twenty-four hours or so. It seems likely that they were due to the production of right ventricular strain (14). The possibility that the infarct might produce pulmonary vasoconstriction was

suggested because relatively small lesions seemed capable of producing extensive effects (4). Experiments on dogs showed that atropine and papaverine were definitely beneficial; the inference being that they abolished the supposed pulmonary vasoconstriction (1). The vasospasm might explain the severe effect on the right ventricle without evidence of infarction at all (10). It seems reasonable to invoke the sudden dilatation of the right ventricle, resulting from physiological strain, as the pathological cause. Clinical and experimental embolism provide grounds to support this suggestion (15).

2. *The Pulmonary Reflex.* Experimental pulmonary embolism in dogs with sago granules caused a diminution in the flow of blood in the right coronary artery (12). But recent experiments on dogs have shown that the changes in the electrocardiogram occur even when the vagi have been severed, and do not disappear after cutting intact vagi. In fact, the curves produced are the same whether the vagi are severed or not (13). The evidence seems convincing that no vagal pulmocoronary reflex exists (13, 15)

3. *Shock.* When much shock was present the curves discovered by McGinn and White were twice as common as in those cases who did not develop shock (6). Shock will reduce the aortic blood pressure, and so will gross obstruction in the pulmonary circulation. The two factors are likely to be present together. The right ventricle in these circumstances will be overloaded and suffering from anoxia. If the right coronary artery is unhealthy the embarrassment will be aggravated.

4. *Anoxæmia* may result from the obstruction in the pulmonary circulation and so affect the myocardium. It is suggested that the coronary anoxæmia may be so severe that ischæmic changes occur in the myocardium. Fairly recent changes of this nature, patchy in distribution, have been found. There had been recurrent embolism, so some time had elapsed. The suggestion was that dilatation of the right ventricle might cause a deficient flow in the right coronary artery and so produced ischæmic changes posteriorly (16). If the coronary arteries are diseased, the changes are all the more easily produced. But definite infarction of the ventricles has been found after pulmonary embolism without any actual coronary occlusion. So it is clear that deficiency, without

actual abolition of blood supply, may suffice to produce these changes (17).

5. *Intraventricular Pressure.* The severe rise in pressure in the right auricle may cause congestion of the coronary sinus and so obstruct the coronary venous flow. This does not seem to be an important point. Ligation of the coronary sinus has even been suggested to improve the coronary circulation in angina pectoris.

CONCLUSIONS. If one may exclude cardiographic changes due to antecedent ischæmic myocardial disease, the fact that the curves peculiar to pulmonary embolism are so transient makes it unlikely that they are due to gross irreversible pathological changes, such as are found in myocardial infarction. Ischæmic myocardial disease, when posterior, is found in the left ventricle, never in the right. In pulmonary embolism it is obviously in the right ventricle that one must look for the causes. The changes in the T waves of *the precordial leads, when* CR_1 *and* CR_2 *are used, point this way.* There is acute overload from thrombotic obstruction and perhaps pulmonary vasospasm causing severe engorgement and dilatation. The oxygen supply is diminished by anoxæmia, and the low aortic pressure due to shock, and pulmonary obstruction. There is, in these circumstances, adequate physiological cause for the curves associated with pulmonary embolism, which are, in consequence, often transient. Minor and perhaps reversible pathological ischæmic myocardial defects produce the curves which last longer than the acute phase of embarrassment. The less common permanent *abnormalities may be associated with the antecedent* presence of coronary disease, which will render them more likely to appear. Associated myocardial disease causes anomalous curves.

Treatment. Venesection should be done if the venous engorgement increase rapidly to a severe degree. Minor grades are usually transient. Up to a point a raised filling pressure is an advantage and may be left alone.

In the acute phase, papaverine (gr ½ to 1, by intravenous injection) appears to have definite value (2). Morphia would be indicated for the pain and dyspnœa. Trinitrin may relieve the pain. *Oxygen is these cases is of very little use, for the cyanosis* is mainly due to the pulmonary obstruction.

Embolectomy from the pulmonary artery might be useful if one could be sure one would find the clot there. But in acute cases

there is no time, and quite severe disturbances may arise from small emboli in the lungs.

Attention is more likely to be focussed on the source of the embolus. This often comes from phlebothrombosis of the legs. When pulmonary embolism is diagnosed, latent thrombosis in the legs should be borne in mind. Slight swelling, cyanosis, tenderness, often over the popliteal veins or lower still, should be sought. Apart from the acute unexpected fatal embolism, death usually results from the third or fourth attack. Since subsequent attacks are likely and dangerous, it seems logical to use heparin and dicoumarol at once (18), continuing the former for two days until the latter acts (see p. 214). If it is certain that there is thrombosis in the leg, ligature of the femoral vein on that side is becoming widely adopted in the United States, and is not difficult to do under focal anæsthetic. It would be worth doing after a second attack. Prophylactic exercises for the knee and ankle joints, with massage to the calves in particular, should *prevent* the stasis which leads to the thrombosis. A pillow should not be placed in the bed beneath the calf

REFERENCES

1 McGinn White (1935) *J Amer med Ass*, **104**, 1473
2 Megibow *et al* (1943) *Arch intern Med*, **71**, 536
3 Wood (1941) *Brit Heart J*, **3**, 21.
4 de Takats *et al* (1939) *Surg* 6 339
5 Megibow *et al* (1942) Surg, 11 19
6 Murnaghan, McGinn, White (1943) *Amer Heart J*, **25**, 573
7. White (1940) *Amer J med Sci*, **200** 577
8 Shirley-Smith (1938) *Quart J Med*, **25**, 85
9 Sokolow (1940) *Amer Heart J*, **19** 166
10 Lewis (1944) *Brit Heart J*, **6** 161
11 Langendorf Pick (1939) *Acta med Scand*, **90**, 289
12 Hochrein, Schneyor (1937) *Münch med Wschr*, **49**, 1929
13 Malinow Katz, Kindo (1946) *Amer Heart J* **31**, 702
14 Semisch Mervles (1942) *Arch intern Med*, **69**, 417
15 Love *et al* (1938) *Ann intern Med*, **11**, 2109
16 Horn *et al* (1939) *Arch intern Med*, **64** 298
17 Currens (1942) *Proc Staff Meet Mayo Clin*, **17**, 502
18 Hampton *et al* (1945) *Bull Johns Hopkins Hosp*, **76**, 245

Pulmonary Disease

Emphysema. The effect of emphysema on the heart has received a good deal of attention in recent years. To begin with, difficulties arise in deciding clinically to what extent emphysema may be present. As far as the lungs themselves are concerned, the important histological changes are loss of elastic tissue, in-

in the size of the alveoli with atrophy and disappearance of their walls, and consequent obliteration of their capillaries. The lungs are enlarged as a result, and give the characteristic appearance of hypertrophic emphysema. This has been contrasted with similar alveolar changes in small lungs, atrophic emphysema. It is doubtful whether the large barrel chest, with large hyper-resonant lungs, is always a true sign of emphysema; it should be more correctly diagnosed as pulmonary hypertrophy (1). In addition, in a certain proportion of cases arteriolar obliteration is present as well as the changes in the capillary bed, possibly as a result of a raised pressure induced by them. These variable features may account for some of the discrepant ideas abroad.

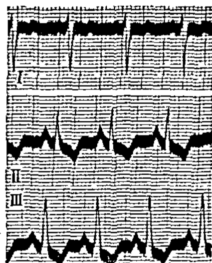


FIG 26
Pulmonary disease From the case shown on Plate 21 right axis deviation

THE SIZE OF THE HEART. AUTOPSY FINDINGS. In one series of 32 cases the right ventricle was found to be enlarged in 75 per cent, and in nearly half it had failed (2). In another series of 45 cases, uncomplicated by hypertension or other lesions, the right ventricle was enlarged in nearly a third. Here the diagnosis of hypertrophy was based on the thickness of the right ventricular wall, which is not an easy thing to measure accurately (3). But the results agreed fairly well with those of another investigation where the ventricles were weighed separately (4) In another series, the patients were selected in rather a different way, for they came into hospital with heart failure, which was presumed to be due to pulmonary disease, the 32 cases of emphysema nearly all had right ventricular hypertrophy (5).

ASSOCIATED ENLARGEMENT OF THE LEFT VENTRICLE. It is not uncommon to find this. It was present in 60 per cent of the last series. Here cases with coronary disease and hypertension were carefully excluded. If this be so, the cause for the associated

enlargement of the left side is obscure, but one must suspect that the possibility of an accompanying hypertension in emphysema is not always successfully discounted.

X-RAY FINDINGS Certain modifications in the shape of the shadow of the heart in emphysema introduce possibilities of error in the estimation of its size. The diaphragm is usually low in position, near the position of full inspiration. When the diaphragm descends the heart descends too, and also rotates to the right on its long axis. The result is that the shadow is small in diameter. The outline is similar to the vertical or "dropped hearts" seen in persons with long narrow chests. In emphysema, of course, the chest is wide and the ribs horizontal, so that, on comparing the size of the thoracic and cardiac diameters, the heart shadow appears smaller than ever. Another factor which may contribute to the apparent small size of the shadow is restriction of the venous inflow, which in asthma may to some extent resemble that induced by Valsalva's experiment (6) (7) In another series a vertical heart was not found so often (8). In about 40 per cent of these cases there was radiological evidence of enlargement of the branches of the pulmonary arteries, with which might be associated enlargement of the main trunk. In about 40 per cent the conus pulmonalis of the right ventricle was enlarged In about half of these the body of the ventricle was enlarged. Only about 14 per cent showed enlargement of the right auricle. It is clear that the enlargement spreads backwards, as it were, affecting first the branches, then the stem of the pulmonary artery and so on along the "outflow tract" of the right ventricle, the right auricle being affected last of all. (Plate 21.) The results agree fairly well with those of one autopsy series (3) It is clear that the right ventricle is not enlarged, as a rule, in emphysema, nor in asthma and emphysema (7). Enlargement of the heart as a whole is often due to associated lesions; but in some cases the increase in size of the left ventricle lacks explanation.

CLINICAL FEATURES Some symptoms and signs which suggest a cardiac origin can be explained in other ways. The dyspnœa is due to the decreased vital capacity. The cyanosis is due to deficient oxygenation in the lungs. The arterial oxygen saturation may be from 70 to 35 per cent (11). Clinical examination of the heart is obviously difficult. The presence of right axis deviation in the

cardiogram is only found in about one-third of cases (Fig. 26); and in some instances the evident enlargement of the right side was accompanied by no changes in the cardiogram (8). In another series 13 per cent showed right axis deviation (9). But in some patients heart failure of the right ventricular type comes on—44 per cent in one series (2). The output of the heart is high, 6 to 10 litres (12). The development is usually terminal and intractable. Cyanosis often becomes intense and polycythæmia high. This is probably due to stimulation of the bone marrow (10). The blood increases in viscosity and this may further embarrass the circulation. *Although dyspnœa is severe, nocturnal attacks and* Cheyne-Stokes respiration are uncommon (5). There is a steady progress downhill and death occurs after a period of coma. The heart rhythm usually remains normal.

Patients with emphysema and bronchitis often have violent paroxysms of coughing which end in syncope, probably from anoxæmia.

The association of the clinical findings, radiological appearances and the weights of the right ventricle at autopsy need further correlation. The question is why some cases fail and not others. Is it actually the severity of the capillary obliteration which is important, or are associated changes in the pulmonary arterioles decisive? In not a few instances the infection gains the upper *hand, and a bronchopneumonia develops. This is particularly* likely to be the end if there has been bronchiectasis.

TREATMENT. Oxygen is the primary and dominant need. If the cyanosis can be relieved, the call for the raised cardiac output may be diminished. An oxygen tent seems the most practical method.

Venesection should not be undertaken too readily, for a high filling pressure is needed to maintain the high output. Digitalis may be harmful in these cases owing to its effect of lowering the venous pressure. The same applies to cardophyllin. *Failure is often* precipitated by infection for which penicillin will probably be needed.

REFERENCES

1. DAVIDSON (1936). *Proc. Roy Soc. Med*, 29, 1315.
2. PARKER (1940). *Ann intern Med*, 14 I, 795
3. GRIGGS, *et al* (1939). *Amer Heart J*, 17, 681.
4. KOUNTZ, *et al* (1936). *Amer. Heart J.*, 11, 163

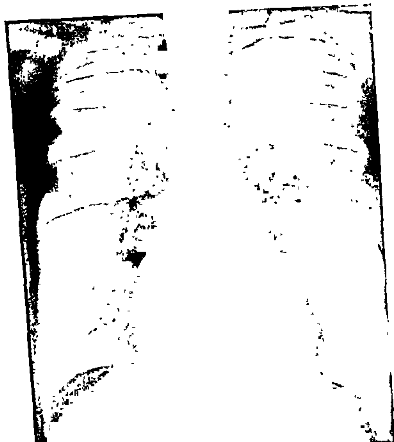


PLATE 21

Chronic Pulmonary Disease.

Showing enlargement of conus arteriosus and of the right auricle

To face p. 162





A



B

PLATE 22

Funnel Sternum.

(A) *Suggestion of enlargement, particularly in the conus pulmonalis.*

(B) Lateral view showing depressed sternum.

5 SCOTT, GARVIN (1941) *Amer Heart J*, 22, 56
6 KERLEY (1935-36). *Proc Roy Soc Med*, 29, 1307.
7. RUBIN (1936) *Lancet*, 2 1059
8 PARKINSON, HOYLE (1937) *Quart J. Med*, 6 59.
9 [illegible] (194[illegible]) [illegible] 228, 113.
[illegible] *Med*, 13, 123.

Pneumoconiosis. The widespread bilateral fibrosis of the lungs in pneumoconiosis affects the pulmonary circulation. In about half the patients there was hypertrophy of the right ventricle at autopsy (1). A chronic form of congestive heart failure came on in about the same number of patients, in whom there was no other form of cardiac or pulmonary disease. These figures agree with those of another series as regards the enlargement of the right ventricle. Right axis deviation was present in the cardiogram in about 40 per cent. One-third died of right ventricular failure. Enlargement of the pulmonary artery appeared in the skiagram, and the loud second sound showed that the tension in it was high. There was some degree of cyanosis, but no polycythemia, in fact, there was a tendency to anæmia (2).

In this form of pulmonary disease the incidence of right ventricular failure appears to be higher than in emphysema.

Unilateral pulmonary fibrosis associated with bronchiectasis caused right ventricular hypertrophy in 16 per cent (1).

Phthisis. Cardiac involvement here is slight in steadily progressive cases. It is rare for the right ventricle to be enlarged, and rarer still for it to fail. Electrocardiographic abnormalities are uncommon (1). Right and left axis deviation were equally infrequent, occurring in only 9 per cent (3). The rhythm is usually normal, but auricular fibrillation has been reported (4). Curves of anterior infarction were recorded in one case where the anterior descending artery was involved in a caseous mass, which replaced half of the anterior wall of the left ventricle (5).

The course of this disease is often hardly long enough to affect the cardiogram, or to cause right ventricular enlargement. Possibly the wasting and toxæmia prevent its development. Chronic fibroid phthisis may cause the usual cardiac complications.

Malignant Infiltration. Widespread malignant deposits may arise in the lungs, in the form of miliary nodules, caused by arterial

embolism (6). In another case the route of invasion was by the lymphatics, which may cause thrombosis in the arterioles (7).

In these cases the right ventricle became enlarged and there was progressive failure. The pulmonary artery was enlarged. In one instance, where thrombosis occurred, the failure suddenly became much worse. In another case there was pronounced atheroma of the pulmonary arteries in addition to the dilatation and enlargement of the right ventricle (8).

REFERENCES

1. GRIGGS, COGGIN, EVANS (1939). *Amer. Heart J*, 17, 681
2. COGGIN, *et al* (1938) *Amer. Heart J*, 16, 414
3. HOPE GOSSE, WINGFIELD (1937). *Brit J Tuberculosis*, 31, 92.
4. ROSENBLATT (1938) *Amer Heart J*, 15, 114
5. SCHNITZER (1947) *Brit Heart J*, 9, 213
6. MASON (1940) *Arch, intern Med*, 66, 1221
7. BRETT, ROBERTSON (1937). *Arch. intern Med*, 60, 1043
8. FISHMAN, *et al* (1945) *Amer Heart J*, 30, 309

Deformities of the Chest

These may be divided into two classes. Those affecting the spine and those affecting the sternum. The latter may be associated with mild degrees of the former.

1. Kyphosis and Scoliosis.

> "and in them, if the hump is above the diaphragm, the ribs are not able to increase in wideness, except to the front, and the chest becomes pointed and not broad; and they become dyspnœic and hoarse For the cavities which receive and send forth the air have not free space." (Hippocrates on Joints, xli.)

A moderate degree of lateral curvature of the spine, usually associated with some kyphosis is very common To the inexperienced, the unusual position of the shadow of the spine may at first introduce difficulties in diagnosis on screening. Except for this it has no importance.

When the curvature amounts to a deformity it is of cardiological interest. Above the diaphragm pure scoliosis with convexity to the right is commoner (1, 2). When this is present the left border of the heart tends to assume the generally convex outline associated with mitral stenosis (2, 3). The heart tends to be displaced somewhat to the left. This may simulate enlargement (3).

In the less common type of scoliosis, with the convexity to the left, the aortic shadow is widened and the knob is prominent (2).

The cardiograms are usually normal. But in one series there was right axis deviation in about one quarter of them (2). This was also found to be the case in about a quarter of the patients with a right dorsal and left lumbar convexity; while left axis deviation was present in about one-sixth of those with left dorsal and right lumbar convexity. There was, in fact, *some degree of rotation* either in the longitudinal or antero-posterior axes of the heart. Precordial leads are very unsatisfactory because of the difficulty of placing the contacts correctly on the deformed precordium.

[illegible] may be linked

and position of the heart shadow.

In a series of five cases which came to autopsy the right ventricle was hypertrophied in four, and right axis deviation had been present in three. All had had cyanosis, œdema, and *orthopnœa* (4).

The important effect of these deformities is on the lungs. The vital capacity tends to be very low, as Hippocrates pointed out. It is about half the normal volume, and this is the cause of the dyspnœa. The circulation rate and venous pressure are *found to be within normal limits, if there is no failure of the heart (1).* The chest does not grow with the individual if the lesion occurs early in life (5). The respiratory *movements* play an important part in the filling of the heart, and the lack of the efficient *action* of the respiratory pump may hamper the venous inflow. More important is the presence in *some cases* of chronic pulmonary lesions, such as fibrosis *or* shrinking on one side with emphysema on the other. *They* are, no doubt, the *cause* of the cyanosis in many patients (1). Syncopal attacks are not uncommon. Later on these *pulmonary* changes *may* overload the right ventricle and cause it to *hypertrophy and bring about its ultimate* failure (4, 5). Accounts of the heart failure of the hunchback have long been conspicuous in *continental* literature. When failure is present these patients tolerate morphia very badly, and quite small doses are dangerous and *may* cause death (6).

In spite of gross *deformity*, it is surprising how in many cases the right side of the *heart* is but little *affected*. These patients

embolism (6). In another case the route of invasion was by the lymphatics, which may cause thrombosis in the arterioles (7).

In these cases the right ventricle became enlarged and there was progressive failure. The pulmonary artery was enlarged. In one instance, where thrombosis occurred, the failure suddenly became much worse. In another case there was pronounced atheroma of the pulmonary arteries in addition to the dilatation and enlargement of the right ventricle (8).

REFERENCES

1 Griggs, Coggin, Evans (1939) *Amer Heart J*, 17, 681
2 Coggin, *et al* (1938) *Amer Heart J*, 16, 414
3 Hope Gosse, Wingfield (1937). *Brit J Tuberculosis*, 31, 92.
4 Rosenblatt (1938) *Amer Heart J*, 15, 114
5 Schnitzer (1947) *Brit Heart J*, 9, 213
6. Mason (1940) *Arch, intern Med*, 66, 1221
7 Brett, Robertson (1937). *Arch intern Med*, 60, 1043
8 Fishman, *et al* (1945) *Amer Heart J*, 30, 309

Deformities of the Chest

These may be divided into two classes. Those affecting the spine and those affecting the sternum. The latter may be associated with mild degrees of the former.

1. Kyphosis and Scoliosis.

"and in them, if the hump is above the diaphragm, the ribs are not able to increase in wideness, except to the front, and the chest becomes pointed and not broad; and they become dyspnœic and hoarse. For the cavities which receive and send forth the air have not free space." (Hippocrates on Joints, xli.)

A moderate degree of lateral curvature of the spine, usually associated with some kyphosis is very common. To the inexperienced, the unusual position of the shadow of the spine may at first introduce difficulties in diagnosis on screening. Except for this it has no importance.

When the curvature amounts to a deformity it is of cardiological interest. Above the diaphragm pure scoliosis with convexity to the right is commoner (1, 2). When this is present the left border of the heart tends to assume the generally convex outline associated with mitral stenosis (2, 3). The heart tends to be displaced somewhat to the left. This may simulate enlargement (3).

CHAPTER VI

THE HEART AND CIRCULATION

In Pregnancy, Thyroid Disorders, Myxœdema, Anæmia, Polycythæmia

In this chapter several diseases are considered together, which have not, at first glance, much in common. But this is less the case than it appears. Both in thyrotoxicosis and pregnancy the heart is overloaded, and there are more or less pronounced changes in the hæmodynamics of the circulation. The same applies to anæmia, where there are, in addition, pathological changes in the myocardium. How far these last occur in myxœdema may still be uncertain; but the circulation in general is much affected. Polycythæmia vera provides a contrast to these last two.

The Heart and Circulation in Pregnancy

There are two distinct problems in cases where heart disease is complicated by pregnancy; the first is whether it is safe to allow the patient to become pregnant; the second is the management of the case during pregnancy and labour.

Effect of Pregnancy on the Normal Heart. There is an increase in the blood volume (1). This is found both in the plasma and the total blood It starts early and reaches its maximum in the ninth lunar month, decreasing a little in the last few weeks. The increase is in the region of 13 per cent (2).

The output of the heart is increased. This starts in the fourth month and may increase to 50 per cent (3) There tends to be a decrease in the last month. These two adjustments are no doubt associated with the increase in the circulatory bed due to enlargement of the uterus and the formation of the placenta. There is a increase in the arteriovenous oxygen difference, indicating an increased utilisation of oxygen

blc

are on the whole much more prone to pulmonary infections than failure of the pulmonary circulation.

2. **Deformities of the Sternum.** These take the form of funnel chest or "Trichterbrust." They are important because their presence may lead to an incorrect diagnosis of heart disease. Clinically it is difficult to estimate the size of the heart, and often in the cases of deep sternal depression spurious enlargement may be simulated. The heart is displaced somewhat to the left and a little upwards. The narrowing of the space between the back of the sternum and the front of the spine causes the heart to become flattened. In the skiagram this produces a wide shadow with a full left border (7). (Plate 22.) The flattening and consequent increase in transparency of the heart is most noticeable in the moderate degrees of sternal depression. The displacement is most conspicuous in the deep funnel types. Examination in the oblique views will contradict the impression of enlargement seen in the anteroposterior view. Measurement with calipers shows that in cases of sternal depression the external diameter from the bottom of the depression to the back of the spine at the same level does not exceed 6⅜ inches (8). Murmurs, systolic in time, are not uncommon in these patients, particularly in the pulmonary area. Not infrequently the patients are of thin weedy build with poor musculature and small chest expansion, and they have, in consequence, a poor capacity for vigorous exertion and easily become breathless. But their hearts are perfectly healthy and in no way inefficient because of the flattening. The danger is that an incorrect diagnosis of heart disease be made, owing to the spurious suggestion of enlargement, and perhaps the presence of harmless murmurs, with a result that the growing child or young adult is forbidden activities which might improve his development, and he suffers all the other disadvantages of a person with a defective heart.

REFERENCES

1. Chapman, *et al* (1939) *Medicine*, 16, 167
2. Pdeiken (1933). *Amer J med Sci*, 189, 99
3. Adam, White (1945) *Amer Heart J*, 29, 440
4. Kerwin (1942) *Arch intern Med*, 69, 640
5. Herzog, Manz (1943). *Amer. Heart J*, 25, 399
6. Daley (1945). *Brit Heart J.*, 7, 101
7. Edeiken, Wolferth (1932) *Amer J med Sci*, 184, 445
8. Evans (1946) *Brit. Heart J*, 8, 162

enlargement. There is often a systolic murmur at the apex, and the mitral first and pulmonary second sounds may be accentuated. There may be slight indentation of the œsophagus by the left auricle (1). There are therefore grounds for a mistake in diagnosing mitral stenosis. The pulse may suggest aortic reflux. The tendency to breathlessness and œdema of the ankles may be assigned to a supposed lesion.

Assessing the Risk. When the diagnosis of mitral stenosis, for example, has been ascertained, the capacity of the patient's heart to go through pregnancy must be gauged. The response to effort is the most important point. Patients may be graded in three classes.

1. Those who are not limited in their ordinary activities.

2. Those whose activities are restricted; these may be subdivided into those who are only moderately affected, and the severely incapacitated.

3. Those who show actual signs of heart failure or have a history of heart failure.

The addition of an aortic lesion to the mitral stenosis does not in itself matter. The question of enlargement is, however, important. The less the better, and aortic lesions tend to cause considerable enlargement (9). Auricular fibrillation is always a very serious complication (10).

When the patient is not a primigravida, the experience of the last pregnancy and the state of the heart afterwards, give very useful indications for the future course.

Patients whose activities are restricted need to be *judged* carefully as individuals. The points to be considered are (1) the degree of incapacity. Any woman who cannot do her housework should *not* undertake pregnancy. (2) The *number* of previous pregnancies and what occurred in them. (3) The *age* (11). (4) The possibility of rest and relief from household duties. The social and economic status is *important* here. Dyspnœa on exertion in the early months points to a considerable risk, and necessitates a reduction in activity. After the third pregnancy the risk rises, even if the former ones have been well tolerated. This point tends to introduce *the age* factor, for after thirty-five the risk is doubled (11). The lesions are now usually getting more severe, and labour may be prolonged. When the response to

pulse pressure increases, as the diastolic falls a little. The possibility of a sort of arteriovenous anastomosis existing in the placenta has been considered as one of the causes of these changes. It has been noted that the venous pressure in the leg is considerably higher than in the arm when the patient is supine; it seems unlikely that pressure from the gravid uterus is the sole cause, for this difference remains in pregnant bitches when the abdomen is opened.

The rate of the circulation, measured by cyanide, is not increased. The lungs are rather more distended, their fields are wider on the skiagram, the costal angle becomes wider as the uterus enlarges, and the diaphragm rises There is actually a slight increase in the vital capacity, but the need for increased ventilation outweighs this, and so gives rise to dyspnœa (5). The viscosity of the blood is slightly diminished.

All these observations give physiological grounds for the long accepted conclusion that pregnancy increases the work of the heart, quite apart from the indirect effect of the increase in the weight of the body. There is, however, some lightening of the physiological load in the last month. The lower level of the fundus of the uterus at this time assists respiration.

Enlargement of the heart does not normally occur. Hypertrophy is never found in other mammals such as bitches, cats, and guinea pigs (6). The upward displacement and the increase in the force of the beat has led to errors in this respect. The electrocardiogram shows some degree of left axis deviation. It is not uncommon to see a Q wave in lead III, with a negative T_3. These tend to disappear after pregnancy, for they are due to upward anticlockwise rotation of the electrical axis of the heart. But they may have been there before, if the patient is of stout thickset build.

Incidence of heart disease in pregnancy. Heart lesions seem to occur in about 2 per cent of cases (7) (8) Mitral stenosis is found in about three-quarters of these. Auricular fibrillation was found in only 3 per cent. Paroxysmal tachycardia is uncommon, and does not increase the risk. Quinidine is not contra-indicated if i ... 36.

... t lesions may be

fal ... us suggestion of

needs careful gauging. The liver may be difficult to feel. Engorgement of the jugular veins is important, but persistent basal crepitations are the most significant. Absolute rest in bed and digitalis are needed. It is best not to interfere with the pregnancy. The uterus will empty spontaneously if the failure is severe (14).

LABOUR AND DELIVERY. This is best done in hospital or nursing home. Usually labour is easy. If the patient reaches term in good condition, she may be expected to go through labour safely. If death occurs at or soon after delivery, prenatal care has probably been inadequate Hence its extreme importance. The first day post partum is the most dangerous (15). But a fatality at this time is unusual. If there has been failure, labour should be as short as possible Forceps may be applied as soon as full dilatation has occurred. If there is any obstetrical reason for supposing that labour will be difficult, Cæsarian section should be done.

AFTER EFFECTS OF PREGNANCY ON THE HEART. Probably most women with heart disease can have one or two children safely, particularly in the early twenties. Repeated pregnancies tend to cause breakdown But it is remarkable how often one sees patients in the forties, in the later stages of rheumatic heart disease, who have had several children and been none the worse. The interval between pregnancies is an important point: if short, the risk increases. But the matter does not end with parturition. The care and rearing a family imposes a stress and strain which is probably more severe, in these days, than gestation and labour.

STERILISATION. This is indicated if there has been failure or threatened failure If one child has been achieved, perhaps with difficult[illegible]
rate f[illegible]
and h[illegible]

REFERENCES

1 HOLLANDER, CRAWFORD (1943) *Amer Heart J* 26 364
2 JEFFERSON *et al* (1938) *Amer J Obst Gyn*, 36, 48
3 STANDEN, CUDDEN (1932) *ibid*, 24, 13
4 BURWELL *et al* (1938) *Arch intern Med* 62 979
5 COHEN, THOMSON (1939) *J Amer med Ass* 112, 1556
6 LEESE SLEETH (1938) *Amer J Physiol* 122, 34
7 CARR HAMILTON (1933) *Amer J Obst Gyn*, 26, 824
8 LAMB (1934) *Amer J med Sci*, 187, 177.
9 HARRIS (1937) *Lancet* 1 677
10 BRAMWELL (1939) *Lancet*, 1, 629
11 [illegible]

exertion is normal, the patient may become pregnant, and go through without harm.

INDICATIONS FOR PROHIBITING PREGNANCY. There are three absolute indications. Heart failure, auricular fibrillation, and active rheumatism. The last is only a temporary contra-indication.

Management of Pregnancy. This falls into two periods. The first is up to the sixteenth week when abortion is comparatively easy. The second is the later period when induction of labour is a serious procedure, and generally to be avoided.

In the *early months* the patient should be kept under careful observation, so that any indications of commencing heart failure are noted. Full instructions of the daily regime, with an afternoon rest and a long night in bed, must be given. With some patients very detailed instructions are essential. Undue increase in dyspnœa and crepitations at the bases of the lungs are the first indications of approaching breakdown. If failure threatens, the patient should stay in bed and be given a full course of digitalis.

In the middle months of pregnancy a sudden acute failure with intense engorgement of the pulmonary circulation leading to severe pulmonary œdema and hydrothorax may take place. This is due to failure of the left auricle, labouring under the load of increased blood volume and raised right ventricular output, to overcome the mitral stenosis (12).

Indications for Terminating Pregnancy. If the signs of failure come on in the early months, the pregnancy should be terminated as soon as they have been cleared up. Sterilisation can be done at the same time. Abortion should be performed on any patient in whom the contra-indications for pregnancy given above are present, when seen for the first time. Termination should be considered in a multipara who has had difficulty in the previous pregnancy.

CARE DURING THE LATER MONTHS. The same precautions should be maintained. During the last two months, a day a week in bed is wise. The heaviest load is in the seventh and eighth months. About this time failure is likely to come on. Often it may be wise to confine the patient to bed during the last two or three weeks. The "last straws" are over-exertion, fatigue, and inter-current infections such as influenza or bronchitis (13). As most healthy patients are now dyspnœic, the abnormal increase in severity

That thyroxin acts directly on the muscle fibres is proved by the increase in beating it produces in embryonic hearts, before the nerves have formed. Even in fragmentary tissue cultures fibrillation has been induced (6) It seems likely, therefore, that the over-action of the heart is not just a response to raised metabolism, but the result of direct action of thyroxin on the heart muscle (7).

Effects on the Peripheral Circulation (8). All the methods of estimating the circulatory rate agree in showing that this is increased. There is an increase in the volume of the circulating blood to as much as 30 per cent. (9) This change appears to be associated with the increase in the cross-section of the vascular bed, due to the general vaso-dilatation. Studies with the plethysmograph show that there is an increase in the average flow of blood in the forearm and leg at rest (10). The peripheral blood flow is thus increased, and more blood reaches the skin, which is flushed and warm. When histamine is pricked into the skin the opening up of new capillaries is relatively slight compared with those of controls, suggesting that nearly all are already open (11). This may be a means of eliminating the increased heat formed as a result of the raised metabolism After exercise there is a much greater flow of blood to the periphery than normal; the muscles need more oxygen, as shown by the increased amount used (12). The peripheral resistance is low. The systolic pressure is usually raised, due to the increase in the force of the heart beat. The diastolic pressure is variable, sometimes low, sometimes raised. The pulse pressure is, in any case, high. These causes account for the bounding character of the pulse. A "capillary pulse" in the small venules can usually be seen. The rapid flow of blood leads to a decrease in the arteriovenous oxygen difference. There is an increase in the rate of the return of the blood to the heart.

It would appear that the chief circulatory adjustment achieves extra dissipation of heat, so that the temperature of the body, measured in the rectum, is kept constant. In addition, the extra demands of the tissues for oxygen are satisfied. An increase in the vital capacity of the lungs allows for extra ventilation.

All these changes are parallel to the rise in the B.M.R.

Abnormalities in the Heart. Clinically it is by no means easy to determine the size of the heart, for the increase in the force of the apex beat suggests enlargement. It is sometimes

12. BRAMWELL, JONES (1944). *Brit. Heart J.*, 6, 129
13 HAMILTON (1937). *Amer. Heart J.*, 14, 653
14 DONOVAN (1936) *Brit med J.*, 1, 104.
15. HOFFMAN, JEFFERSON (1942). *Amer J. med. Sci.*, 204, 157.

The Heart and Circulation in Thyroid Disorders

"There is one malady which I have in five cases seen coincident with what appeared to be enlargement of the heart... the malady to which I allude is enlargement of the thyroid gland." (C. H. Parry, 1825.)

Hyperthyroidism has a profound effect on the heart and circulation. The increase in the basal metabolism that thyrotoxicosis produces sets the activities of the body at a high level, so that there is an increase in the demand of the tissues for oxygen. *This is met by increasing the flow of the blood*

Effect on the Function of the Heart. The rate of the heart is increased. The tachycardia is persistent. There may be some *slowing during sleep, but observations with the cardiotachometer* over long periods, show that the rate is always higher than normal (1). The sleeping rate tends to be increased in proportion to the basal metabolic rate. The response in the rate of the heart to emotion and exercise is exaggerated and prolonged.

The output of the heart increased up to 50 or 100 per cent in the minute (2). On muscular effort there is an abnormally high and prolonged rise in the output (3). But when failure comes on the heart may not be able to increase its output to this degree (4).

Clinically the abnormal force and vigour of the heart beat are familiar enough. The sounds are excessively loud, especially the first sound at the apex. In addition there may be superficial clicking or scratching noises audible, especially over the base in the pulmonary area. These sounds appear to be produced in the pericardial sac by the abnormal vigour of the heart beat. They may be met with apart from hyperthyroidism.

Systolic murmurs are often heard at the apex, sometimes of the cardio-respiratory type. Usually they differ in quality from case to case, and tend to change with posture.

Perfusion experiments have shown that there is a direct response of the heart to thyroxin (4). The rate of beating remains fast in animals under the influence of thyroxin, even when the sinu-auricular node and the bundle of His have been destroyed (5).

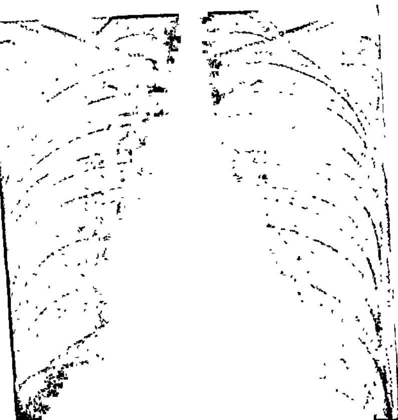


PLATE 23
Heart in Thyrotoxicosis.

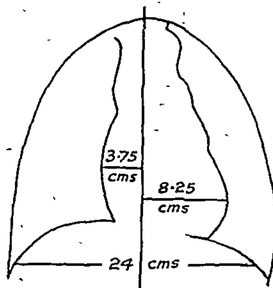


FIG. 27
Outline of heart shadow of elderly patient with thyrotoxicosis (B M R +45), and auricular fibrillation

possible to detect an increase in the pulsation of the pulmonary area due to increase in the size of the pulmonary artery. Actually in mild and recent cases, examination by X-rays shows that the heart is normal in size and shape. But when the symptoms are severe, or of long duration, the left border of the heart becomes straight owing to an increase in *the prominence of the* pulmonary arc. (Fig. 27). The outline thus becomes somewhat similar to that of *mitral stenosis*. There is a difference in that the left ventricle may be enlarged too, so that the heart becomes like a ham in shape. There is no enlargement of the left auricle. The right auricle may be dilated. (Plate 23) In one series, at autopsy almost half the cases showed enlargement (13).

It is not common to find pathological changes on microscopical section. Necrosis, cellular infiltration, and fibrosis have been described, but they are not constant, and are probably due to causes other than thyrotoxicosis.

Auricular Fibrillation. Thyrotoxicosis is an important cause of auricular fibrillation. Auricular flutter is not uncommon. In one large series one-fifth had auricular fibrillation (14). Severe cases fibrillate sooner than mild *The liability to fibrillate depends* on the age of the patient; under thirty it is rare, but it is much more common in the elderly, most cases occurring between fifty and seventy (15); *the nodular variety of goitre found in the* elderly is more prone to it; the onset depends also on the duration of the hyperthyroidism. It is not uncommon for elderly patients to have had a mild degree of thyrotoxicosis for a long time.

The attacks are often paroxysmal at first; the disease was the cause of 15 per cent of cases in one series of paroxysmal fibrillation. Later the paroxysmal attacks are replaced by permanent fibrillation (16). Fibrillation not uncommonly comes on after operation. Thyrotoxicosis causes about 7 per cent of all cases of fibrillation.

Angina and Hyperthyroidism. Most patients complain of palpitation and dyspnœa. Angina pectoris sometimes occurs. These are elderly patients in whom there is coexistent coronary disease, which the overwork of the heart renders more harmful.

Masked or Latent Hyperthyroidism. Although distinctions have been drawn between the hyperthyroidism of younger women (Graves' disease) and that of elderly patients (Plummer's disease), it seems that the main features are the same. It is not the disease that is different, but the patients. For this reason hyperthyroidism in elderly persons is often overlooked. These patients are less prone to show exophthalmos. The eyes, nevertheless, may show some retraction of the lids and a peculiar stare, a "glittering eye." The goitres are often very small, but the gland is hard and nodular; often it is largely below the sternum. Loss of weight is invariable and most important. Subjective symptoms may not be suggestive. The demeanour is jerky and there is usually tremor. The skin is unusually warm and moist for an old person. Cold is remarkably well tolerated, and but few bed clothes are required. Transient glycosuria should arouse suspicion (17). The most constant signs are found in the cardiovascular system The fast bounding pulse and overaction of the heart are always present. An unexplained fibrillation is very common. The result is that these cases may progress to heart failure unless the diagnosis is made, for the elderly heart tolerates hyperthyroidism badly, and fibrillation soon leads to failure. In addition to this the grave deterioration in the general health may severely diminish the possibility of cure.

ELECTROCARDIOGRAPHIC CHANGES. There are no characteristic changes. Sometimes R waves are high and T waves exaggerated (18); or there may be slight inversion of T in leads II and III. There is no relationship to the grade of hyperthyroidism, nor prognostic significance. Abnormal curves show the presence of lesions due to other causes; in this respect, they may be useful.

Treatment. This must aim at eliminating the toxic effect of the hyperthyroidism. If there is fibrillation the need is all the more

reactions include fever, drug rashes, adenitis, and joint pains. With the recent preparations toxic effects appear to be quite rare. Some patients can tolerate the propyl or methyl preparations who are sensitive to others. When toxic reactions occur, the drug must be discontinued, but it may be possible to start again with doses of 0.1 g. daily, and by increasing the dose gradually to obtain a satisfactory result. This does not apply to agranulocytosis, which is a bar to further treatment. The chief danger seems to be precipitation of toxic effects by some acute intercurrent infection, particularly of the throat. Pericarditis and complete heart block have been recorded (24)

SUGGESTED PROCEDURE Since it is clear that a thiouracil preparation is usually the best means of overcoming excessive activity of the thyroid gland, every case of thyrotoxicosis will be treated with some such drug, whether the ultimate aim is control, and perhaps cure, by means of the drug alone, or to make the patient as fit as possible for operation. It seems likely that early cases in young women without much enlargement of the gland may be brought under control, and perhaps restored to normal health by the thiouracil preparation alone. If the condition is severe, and the gland much enlarged and very vascular, it is unlikely that thiouracil will cure. In this case the drug will be used to reduce activity as much as possible, and when it is felt that the maximum benefit has been achieved, the drug will be discontinued, and a course of iodine given for the ten days prior to operation. In elderly women with nodular goitres a thiouracil preparation may sometimes succeed, but when the gland is very large, operation is almost certainly likely to be needed.

If auricular fibrillation is present ...
to be controlled by d...
rhythm may come b...
often require to be la...
in spite of alleviation of the thyrotoxicosis, a course of quinidine may be given. If a state of heart failure has been reached, it will be necessary to treat this before operation is considered. Operation will almost certainly be required in such a patient, nor does previous heart failure contra-indicate it, in fact the reverse is the case.

The general health of these elderly patients is often very poor, and they are bad operative risks from that point of

urgent. Until lately subtotal thyroidectomy after preliminary iodine therapy has offered the best chance of success. Astwood's discovery of the efficacy of thiourea has opened up possibilities of the greatest importance. The disadvantages of thiourea have been diminished by the introduction of thiouracil, and it seems possible that the methyl derivative is more effective and less toxic. No doubt we are only at the beginning of a series of preparations that will prove still more valuable; many are on trial in America.

METHYL THIOURACIL. The dose is usually 0.2 gramme thrice daily, though some prefer not to exceed 0.4 gramme daily. The maintenance dose is from 0.1 to 0.2 daily, but patients can sometimes manage with less. The latent period varies according to the dosage employed, but is a few days shorter than with corresponding doses of thiouracil (19). In a large proportion of cases the activity of the thyroid is reduced, patients gain weight, and lose their symptoms; the B.M.R. falls. As the saturation point is reached the gland may increase in size, and later on signs of myxœdema may appear. Some observers have found that the diffuse hyperplastic gland responds better than the nodular goitre (20, 21). In one series with the methyl derivative there were no toxic effects (22), and in another they were fewer than with thiouracil (19). In a third with the latter there were also no toxic effects (20). In quite a proportion of cases, probably about two-thirds, auricular fibrillation clears up (23). If iodine has been given beforehand the effect of thiouracil preparations appears to be delayed (22).

Propyl thiouracil may replace the methyl preparation, and others are on trial. The dose of the propyl derivation is 50 to 75 mg. daily; the effect is apparent in about four days. The maintenance dose is 25 to 50 mg. daily. No ill effects were noted in 52 cases; some of these had shown toxic reactions with thiouracil (25). Somewhat similar results are reported in a series of 54 cases, 13 of whom had nodular goitre. There was one in whom the fever of drug therapy developed (26). The immediate results compare favourably with those of surgical operations. Time will show the later effects (27).

Toxic Reactions. The only dangerous toxic reaction is agranulocytosis. This is rare, but may develop at any stage and makes it necessary to keep a watch on the white cells. Other

REFERENCES

"The Heart Rate"
Exper Biol and Med., 34, 587.
ns Hopkins Hosp, 46, 203.
exper Med, 77, 631
Amer J Physiol, 98, 357.

t J, 20, 715
t., 18 59
rn Med, 69, 409
eart J 14, 598
vest, 20, 517
J Med, 24, 499
, 195 248

J Med, 24 499.

21 BEIERWALTES, STURGES (1946) *J Amer med Ass*, 131, 80
22 LEYS (1945) *Lancet* 1, 461
23 COOKSON (1945) *Lancet*, 2, 485
24 BAIN (1945) *Brit Heart J*, 7 1
25 ASTWOOD, VAN DER LAAN (1945) *J Clin Endocrinol*, 5, 424
123 1190
Lancet, 1, 241
1, 809
11

The Heart and Circulation in Myxœdema

This subject provides an interesting contrast to the findings in hyperthyroidism. Mild degrees of myxœdema are probably not uncommon, and the more severe types often escape recognition. The onset of the symptoms is so gradual, and the absence of acute disorder, together with the dulled appreciation of the subject, make the patients unlikely to seek medical advice. It is only in the more pronounced degrees of hypothyroidism that the "myxœdema heart" is likely to be found. It is important to appreciate the possible features of this condition, otherwise the diagnosis may be missed and the chance of an early cure lost.

The clinical picture is familiar enough The heavy, puffy, expressionless face; with waxy pallor, and yet curiously bright pink cheeks; sparse, dry hair, dry skin, slow, dull mentality and croaking voice, somnolence, fatigue, and dislike of cold make an *ensemble* that should be easily recognised.

prolonged course of thiouracil, if tolerated, may give them a chance to improve the state of their general health sufficiently *for operation*. Some patients dislike the thought of operation; they prefer to use thiouracil, and may be prepared to continue it indefinitely should this be found necessary. There are some who, after six months or so, are able to leave off the drug and remain in normal health; there are others who tend to relapse. In these instances, operation might be suggested, should the patient feel inclined to face it, or dislike the idea of taking the drug indefinitely. Although it is true that such drugs as digitalis are taken regularly for years, it seems that the thyrotoxic temperament does not like persistent medication, and a certain undercurrent of restlessness, and anxiety about the ultimate outcome, makes them unsuitable subjects for prolonged use of the drug.

In a disease so protean in its manifestations as thyrotoxicosis, where so many variable features present themselves, no hard and fast rules can be laid down. Each case must be considered individually, every important factor being duly weighed.

Thyroidectomy. Before operation the usual course of iodine for ten days should be given. This appears to lessen the liability to hæmorrhage (19). It should be continued after operation as usual, for ten days. Thiouracil should be discontinued before giving the iodine. The previous administration of thiouracil does not interfere with the iodine effect. If iodine has been given previously, the effect of thiouracil appears to be delayed (22). It is important to select an optimum moment, at the time of full medical control. Avertin or paraldehyde and gas and oxygen are the most suitable anæsthetics. Rectal administration may make it possible to conceal the actual day by previous trial enemas, if this is thought to be best for the patient.

Other Drugs. The amino-benzine preparations seem to be more toxic than the recent thiouracil, and have no particular benefit in themselves. It remains to be seen how far radioactive iodine will control the thyroid gland. It appears not to be toxic, and may perhaps prove the ideal line of treatment in the future.

By whatever means it be achieved, elimination of the thyrotoxic effect relieves the heart of its disability, and a return to normal efficiency can be expected in due course, provided no associated lesions are present.

REFERENCES

"The Heart Rate"
Exper Biol and Med, 34, 587.
...ns Hopkins Hosp, 46, 203.
...exper Med, 77, 631
Amer. J Physiol, 98, 357
...J, 20 715
...t, 18 59
...0 ABRAMSON, FIERST (1942) *Arch. intern Med*, 69, 409
...t J, 14, 598
...t, 20, 517.
...Med., 24, 499
...95, 248.
...Med, 24 499
...r med Ass, 131, 80
...lin. Endocrinol, 5, 424
...3 1190
...*Lancet*, 1, 241.
...1, 800
... 11

The Heart and Circulation in Myxœdema

This subject provides an interesting contrast to the findings in hyperthyroidism Mild degrees of myxœdema are probably not uncommon, and the more severe types often escape recognition. The onset of the symptoms is so gradual, and the absence of acute disorder, together with the dulled appreciation of the subject, make the patients unlikely to seek medical advice. It is only in the more pronounced degrees of hypothyroidism that the "myxœdema heart" is likely to be found. It is important to appreciate the possible features of this condition, otherwise the diagnosis may be missed and the chance of an early cure lost.

The clinical picture is familiar enough. The heavy, puffy, expressionless face, with waxy pallor, and yet curiously bright pink cheeks, sparse, dry hair; dry skin, slow, dull mentality and croaking voice, somnolence, fatigue, and dislike of cold make an *ensemble* that should be easily recognised.

prolonged course of thiouracil, if tolerated, may give them a chance to improve the state of their general health sufficiently for operation. Some patients dislike the thought of operation; they prefer to use thiouracil, and may be prepared to continue it indefinitely should this be found necessary. There are some who, after six months or so, are able to leave off the drug and remain in normal health; there are others who tend to relapse. In these instances, operation might be suggested, should the patient feel inclined to face it, or dislike the idea of taking the drug indefinitely. Although it is true that such drugs as digitalis are taken regularly for years, it seems that the thyrotoxic temperament does not like persistent medication, and a certain undercurrent of restlessness, and anxiety about the ultimate outcome, makes them unsuitable subjects for prolonged use of the drug.

In a disease so protean in its manifestations as thyrotoxicosis, where so many variable features present themselves, no hard and fast rules can be laid down. Each case must be considered individually, every important factor being duly weighed.

Thyroidectomy. Before operation the usual course of iodine for ten days should be given. This appears to lessen the liability to hæmorrhage (19). It should be continued after operation as usual, for ten days. Thiouracil should be discontinued before giving the iodine. The previous administration of thiouracil does not interfere with the iodine effect. If iodine has been given previously, the effect of thiouracil appears to be delayed (22). It is important to select an optimum moment, at the time of full medical control. Avertin or paraldehyde and gas and oxygen are the most suitable anæsthetics. Rectal administration may make it possible to conceal the actual day by previous trial enemas, if this is thought to be best for the patient.

Other Drugs. The amino-benzine preparations seem to be more toxic than the recent thiouracil, and have no particular benefit in themselves. It remains to be seen how far radioactive iodine will control the thyroid gland. It appears not to be toxic, and may perhaps prove the ideal line of treatment in the future.

By whatever means it be achieved, elimination of the thyrotoxic effect relieves the heart of its disability, and a return to normal efficiency can be expected in due course, provided no associated lesions are present.

Cardiac Lesions. The pathological changes in the myocardium are variable. In some cases very little has been found, in others a good deal. Interstitial œdema has been described (8). The fibres of the heart muscle may be swollen and appear to press on the capillaries (9) Hydropic vacuolation has been noted, with loss of striation and fragmentation, the staining reaction being poor and variable (10).

Ischæmic fibrosis is common; this is due to the atheroma of the coronary arteries, to which the high level of the cholesterol in the blood no doubt makes the patient prone (11). Macroscopically there may be moderate hypertrophy, and the muscle is pale and rather soft. It will be seen, therefore, that in a proportion of cases pathological changes apparently peculiar to the disease may be found, but due allowance must be made for associated causes, such as ischæmia, hypertension, and also for anæmia.

Pericardial Effusion The presence of pericardial effusions in some cases has aroused some speculation as to how far they may be responsible for the increase in the heart shadow revealed by X-rays. The presence of a considerable effusion has been proved by paracentesis (12) The pressure has been measured, and shown to range from +10 and +10 mm. of water. This is the same as observations on pleural effusions (13). Ascites may be present too, with enlargement of the liver, suggesting a mild degree of tamponade (14) (See Plate 16.)

Treatment with thyroid causes the effusion to disappear (15), but digitalis may be needed if there are causes other than myxœdema.

As the effusion may recur if treatment be discontinued this [illegible]

[illegible] excess fluid has been found (11).

Cardiac Enlargement. It is well known that the heart shadow may be greatly enlarged The beat is feeble and languid. In some cases the increase may be due to dilatation, but in the grosser increases the possibility of effusion must be remembered. Hypertension is not uncommon together with myxœdema, and this may cause some increase in size.

Even if the dilatation is great, return to normal is possible (16). It would appear that reversible enlargement, due either to dilatation or effusion, or both, may b[illegible]

Changes in the Circulation. When the basal metabolic rate is low, the skin is cold and dry. There is a decrease in the peripheral blood flow, per square metre of body surface per minute. As a result there is a diminished flow of blood to the skin (1). The capillaries themselves are affected. Microscopical study shows that only relatively few are open, and their loops are narrow (2). By means of the intravenous injection of fluorescine it has been possible to show that they are abnormally permeable, for an excessive amount escapes even though the number open are few (3). The increase may be in the region of 130 to 165 per cent. These changes may afford an explanation for the presence of true œdema (4).

The diminution of the flow of blood to the skin has the beneficial effect of conserving heat, which can ill be spared when metabolism is reduced. It is the very opposite of the state of affairs in hyperthyroidism.

The arteriovenous oxygen difference is increased; this is linked up with the considerable slowing of the circulation. The circulation is too slow to supply enough oxygen, but the requirements of the tissues are low. The cardiac output falls anything from twenty-five to forty per cent.

The fall in output is shown in the decrease in the stroke and in the minute volume, for the rate of the heart is slow. It has been estimated that only 1.4 per cent of the output went to the skin when the patient was ill. Later this increased to 4 per cent (5). The volume of the circulating blood is reduced by about 15 per cent. The level of the blood volume is related to the oxygen requirements of the vessels, and as these are low, the diminished supply is not harmful (6). The opposite is the case in hyperthyroidism.

There may be quite severe anæmia; simple hyperchromic, hypochromic, or Addisonian hyperchromic, the red cells ranging from 2⅜ to 3 million (7). How far the anæmia may influence the circulatory changes had not been worked out; probably not at all, in view of the lowered oxygen requirements of the tissues. The cholesterol in the blood is high, and keeps fairly parallel with the basal metabolic rate.

All these abnormalities will clear up under thyroid medication.

is the presence of a pericardial effusion, which may cause low voltage curves.

Finally, there must also be considered the possibility of associated coronary disease and the effects of anæmia on the myocardium. The conclusion is that skin, myocardial and pericardial factors may all operate together, or singly, to cause changes in the cardiogram which clear up under thyroid medication. Which may predominate must vary from case to case. The fact remains that characteristic curves are found in most cases of myxœdema

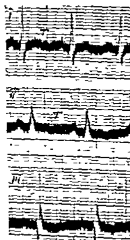


Fig 28A
From a case of myxœdema showing flat T waves

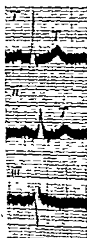


Fig 28B
From the same after taking thyroid, showing increase in T waves

of any severity. It is interesting to note that the flat or negative T wave in hypothyroidism may become upright after the administration of potassium (21)

Congestive Failure. This may be found when severe myxœdema has been present for some time. Actually it is very rare, despite the presence of gross changes in the heart (18). The hæmodynamics of the circulatory failure in these cases have not been worked out It would be interesting to know what happens to the blood volume and the venous pressure The lowered demands of the tissues tolerate an inefficient circulation.

Cardiac Pain. It seems rather a paradox that there was a vogue a few years ago for inducing myxœdema by total thyroidectomy to relieve angina pectoris, and yet thyroid may be given to patients with myxœdema to cure the same symptom. Peel (17) has distinguished two types: one is the usual pain typical of angina of effort. This appears to be associated, for the most part, with independent coronary disease. The other is a more persistent dull precordial ache, which is relieved by thyroid medication and presumably not of cardiac origin. A similar symptom has been noted by Campbell and Suzman (18). One explanation of the cardiac type of pain is that myxœdematous changes are associated with the coronary disease which aggravate the ischæmia due to the vascular sclerosis. This will be cleared up by thyroid (19). It must be borne in mind that thyroid may increase the efficiency of the heart and so improve the coronary circulation. On the other hand, the demands and work of the heart are also increased. Possibly the balance between these two results determines whether thyroid relieves the liability to angina for a time, or makes it worse; which is, in fact, sometimes the case (17).

Abortive Myxœdema Heart. A variety with atypical precordial pain has been described by Zondek (9). It is less common than the others, but its occurrence has been confirmed (17). These patients lack the obvious stigmata of myxœdema; but the basal metabolic rate is low and the cholesterol level in the blood is high. The cardiogram usually suggests myxœdema. The pain is a continuous dull ache. Thyroid relieves the symptoms.

Cardiographic Changes. These are often very characteristic: P waves are small, there is low voltage of Q R S, and the T waves are flat or slightly inverted. There may be slight slowing of auriculo-ventricular and intraventricular conduction (Fig. 28). Under thyroid medication, in a few weeks these abnormalities tend to disappear. Their precise cause has been a matter of debate. One possibility is that the changes in the skin causing increase of resistance give rise to them. By inserting needle electrodes under the skin deflections of rather larger voltage are obtained But this occurs to some extent in healthy persons. With special apparatus, the amplifying electrocardiograph, which measure potentials, the deflections are still found to be small (20). This observation shows that skin changes are not entirely responsible. A further possibility

is the presence of a pericardial effusion, which may cause low voltage curves

Finally, there must also be considered the possibility of associated coronary disease and the effects of anæmia on the myocardium. The conclusion is that skin, myocardial and pericardial factors may all operate together, or singly, to cause changes in the cardiogram which clear up under thyroid medication. Which may predominate must vary from case to case. The fact remains that characteristic curves are found in most cases of myxœdema

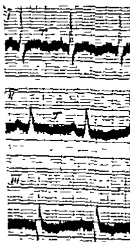


Fig 28A
From a case of myxœdema, showing flat T waves



Fig 28B
From the same after taking thyroid, showing increase in T waves

of any severity It is interesting to note that the flat or negative T wave in hypothyroidism may become upright after the administration of potassium (21)

Congestive Failure. This may be found when severe myxœdema has been present for *some time*. Actually it is very rare, despite the presence of gross changes in the heart (18). The hæmodynamics of the circulatory failure in these cases have not been worked out. It would be *interesting* to know what happens to the blood volume and the venous pressure. The lowered demands of the tissues tolerate an inefficient circulation

Treatment. All observers agree that thyroid medication provides a cure in most cases. But sometimes a patient very far gone in the disease fails to respond. There is general agreement that the initial doses of thyroid should be very small, perhaps only ½-grain of the dry extract daily. The amount should be increased cautiously, in order that angina may not be provoked. The optimum maintenance dose is usually about two or three grains daily, but it may have to be more. Occasionally resistant cases are met with which need much larger doses.

Apart from the possibility of associated coronary disease the prognosis is good. If there is liability to angina, a mild state of myxœdema is beneficial and should be maintained.

REFERENCES

1. Stewart, Evans (1942) *Arch intern Med*, **69**, 808.
2. Zondek, *et al* (1941) *Amer J med Sci*, **202**, 435
3. Lange (1945) *Amer J. med Sci*, **208**, 5
4. McGavack, Lange (1945) *Amer Heart J.*, **29**, 421
5. Stewart, Dietrich, Crane (1938) *J clin Invest*, **17**, 247
6. Gibson, Harris (1939) *J clin Invest*, **18**, 59
7. Bomford (1938) *Quart J Med*, **7**, 495
8. Lerman, Clark, Means (1933) *Ann intern Med*, **6**, 1251
9. Zondek (1941) *Lancet*, **2**, 310.
10. La Duc (1943) *Ann intern Med*, **18**, 332
11. Higgins (1936) *Amer J med Sci*, **191**, 80
12. Schnitzer, Guttman (1946) *Brit. Heart J*, **8**, 25
13. Feasby (1940) *Amer Heart J*, **19**, 749
14. Marzullo, Franco (1939) *Amer Heart J*, **17**, 368
15. Harrell, Johnston (1943) *Amer Heart J*, **25**, 405
16. Evans, Courtenay (1937) *Lancet*, **2**, 1300
17. Peel (1943) *Brit Heart J*, **5**, 89
18. Campbell, Suzman (1934) *Guy's Hospital Rep*, **84**, 281.
19. Fournier (1942) *Proc Staff Meet Mayo Clin*, **17**, 212
20. Scherf, Boyd (1945) "Clinical Electrocardiography"
21. Sharpey-Schafer (1943) *Brit Heart J*, **5**, 85.

The Heart in Anæmia

In anæmia the capacity of the blood to carry oxygen is reduced. When this falls below a certain level for any length of time pathological changes occur in the myocardium and there are also profound changes in the circulation. The result is that a diseased heart is overworked.

The critical level in the hæmoglobin below which these changes become apparent is between fifty and sixty per cent, or about seven grammes of hæmoglobin per hundred cubic centimetres (1).

Myocardial Degeneration. The fatty degeneration of the myocardium has long been recognised in the post-mortem room. The heart is extraordinarily flabby. The muscle has lost all resilience. It is pale, greasy and friable; the fatty streaks are conspicuous under the endocardium of the ventricles, which may appear somewhat dilated. No doubt the degree to which these are apparent depends on the duration of the anæmia. There may be some increase in the weight of the heart.

Changes in the Circulation. These are adjustments which may be due to the demand of the tissues for oxygen, and in a sense they are compensatory to the decrease on the oxygen-carrying capacity of the blood.

The pressure in the right auricle is increased, when measured by the intracardiac catheter, up to 8 to 12 cm. above the angle of the sternum with the patient lying supine. (2). This is in agreement with the clinical observation that the veins in the neck may be conspicuously engorged It must be noted that other observers have not found this rise in right auricular pressure (1).

The *rate of the circulation*, measured from the arm to the face (histamine) is increased (3).

The *cardiac output* is increased according to earlier inhalation methods and confirmed by auricular catheterisation. The rise in litres per minute may reach double the normal level. This high level may be in some degree associated with a tendency to an increase in the heart rate. The raised venous pressure is likely to be associated with the rise in output.

At the periphery there is decrease in the resistance (1). The pulse pressure is raised, so that the pulse is collapsing Capillary pulsation can usually be detected. The skin is warm. There is an increase in the arterio-venous oxygen difference, so that the percentage utilization of available oxygen is high (4) The blood volume is decreased to half the normal figure, or even below (5). This may not be a constant finding, as in one of Nylin's cases it was slightly raised (6) The diminution in the [illegible]

[illegible] heart rate [illegible] account for the rise in output, to which, no doubt, the

Treatment. All observers agree that thyroid medication provides a cure in most cases. But sometimes a patient very far gone in the disease fails to respond. There is general agreement that the initial doses of thyroid should be very small, perhaps only ½-grain of the dry extract daily. The amount should be increased cautiously, in order that angina may not be provoked. The optimum maintenance dose is usually about two or three grains daily, but it may have to be more. Occasionally resistant cases are met with which need much larger doses.

Apart from the possibility of associated coronary disease the prognosis is good. If there is liability to angina, a mild state of myxœdema is beneficial and should be maintained.

REFERENCES

1. Stewart, Evans (1942) *Arch intern Med*, 69, 808
2 Zondek, *et al* (1941) *Amer J med Sci*, 202, 435
3 Lange (1945) *Amer J. med Sci*, 208, 5
4 McGavack, Lange (1945) *Amer Heart J*, 29, 421
5 Stewart, Dietrich, Crane (1938) *J clin Invest*, 17, 247
6 Gibson, Harris (1939) *J. clin Invest*, 18, 59
7. Bomford (1938) *Quart J Med*, 7, 495
8 [illegible] *Med*, 6, 1251
9.
10
11
12
13
14 68
15. 405
16.
17
18 34, 281.
19 7, 212
20 phy"
21.

The Heart in Anæmia

In anæmia the capacity of the blood to carry oxygen is reduced. When this falls below a certain level for any length of time pathological changes occur in the myocardium and there are also profound changes in the circulation. The result is that a diseased heart is overworked.

The critical level in the hæmoglobin below which these changes become apparent is between fifty and sixty per cent, or about seven grammes of hæmoglobin per hundred cubic centimetres (1).

EFFECT OF TRANSFUSION. Transfusion has been the subject of an interesting study by Sharpey-Schafer (2). In view of the raised venous and right auricular pressure this may be dangerous. Whereas in normal hearts, a rise in the filling pressure on the right side results up to a point in a rise in output, in anæmic hearts the output tends to fall. The heart apparently cannot respond to a further rise. Pulmonary œdema may result.

In some cases transfusion seems to be very desirable, if there is no time to lose If it is decided to transfuse, small amounts, up to half a pint, of concentrated red cells may be given slowly. The veins in the neck should be examined carefully for clinical evidence of raised venous pressure. The patient should be well propped up, so that the venous pressure is minimal As digitalis may reduce venous pressure, it is reasonable to use this at the same time, by intravenous injection (12).

With the modern treatment for anæmia, the effect upon the circulation is of practical importance in two other connections. It emphasises the necessity of keeping patients with advanced anæmia rigidly at rest, since otherwise there is risk of sudden death from heart failure. It suggests the advisability of keeping anæmia in mind when a patient complains of cardiac symptoms for which no adequate cause can be found. In some cases of microcytic hypochromic anæmia the state of the blood may be overlooked. T[illegible]

seen in a gooc[illegible]

diagnosis easy[illegible]

REFERENCES

1 BRANNON, et al (1945) J clin Invest, 24, 332
2 SHARPEY SCHAFER (1945) Lancet, 2 296
3 BLUMGART et al (1930) J clin Invest 9 678
4 [illegible]
5
6
7
8
9
10 [illegible] G L (1945) Amer Heart J, 30, 685
11 SZEKELY (1940) Brit Heart J, 2, 1
12 MCMICHAEL SHARPEY SCHAFER (1944) Quart J Med, 13,

raised pressure in the right auricle also contributes. The cause of this in the presence of diminished blood volume is obscure, but might be due to venous vasoconstriction.

Clinical Features. Fatigue, lassitude, giddiness, palpitation, are the minor symptoms. The cardiac symptoms do not become conspicuous until the level of the hæmoglobin has fallen below 50 per cent. Dyspnœa then becomes troublesome, and about a quarter of the patients complain of substernal pain on exertion (7). This seems to depend on the level of the hæmoglobin, for it disappears when the blood improves, unless there is associated disease of the coronary arteries. The dyspnœa does not amount to orthopnœa; patients can lie flat, and the lung fields are clear. Occasionally there is intermittent claudication (7).

Physical Signs. *Cardiac Enlargement* can be demonstrated by X-rays in a certain proportion of cases. It tends to decrease early as soon as there is improvement in the blood (8).

Murmurs. These are usually systolic in time and may be heard at the apex or at the base. They vary a good deal in loudness; usually they are soft and blowing, and change with alterations in posture. It is supposed that they are due to diminution in the viscosity of the blood (9).

Electrocardiographic Changes. The curves are normal in the majority of cases. There may be a slight degree of heart block (7). Slight flattening of the T waves may be seen. Low voltage of the QRS has been noted and some depression of the RS-T junction (2.11). A plateau type of RS-T, similar to that of coronary thrombosis may be found. These minor changes may return to normal on improvement of the blood.

Heart Failure. If the patient has been up and about with the hæmoglobin below 30 per cent, heart failure is likely to come on. This is all the more likely to develop if there is a coexisting valvular lesion, such as mitral stenosis. The liver and veins become engorged and the œdema appears. There now may be orthopnœa. The apex beat becomes weak and diffuse, and a gallop rhythm can often be heard over the right ventricle. It seems likely that this side of the heart is predominantly affected. Basal diastolic murmurs may be audible. We have found these to be associated with enlargement of the pulmonary artery. The failure will clear up, and the murmur will disappear when the hæmoglobin increases.

in the limbs. Associated with the large spleen, presumably, is thrombosis of the splenic vein. In fact, in about one-third of the cases vascular complications arose (6). These patients are prone to gout. There is some association with erythromelalgia.

Gaisbock's Disease. The association of hypertension and polycythæmia is obscure. Some think it may be fortuitous. The constant absence of the splenic enlargement which may be so conspicuous in the other type, is held to mark a difference. The greatly increased viscosity of the blood cannot be a deciding factor, although it is one theoretical cause for a rise in pressure. It must be noted that there is no tendency to a rise in blood pressure in the secondary polycythæmia of congenital cyanotic heart disease, but in this instance, the capillary bed may be dilated. In the polycythæmia hypertonica there is albuminuria, and the usual sequelæ of high blood pressure, arterial and left ventricular hypertrophy.

REFERENCES

1. HADEN (1938) *Amer J med Sci*, 196, 493
2. GIBSON, *et al* (1939) *J clin Invest*, 18, 621
3. STEWART *et al* (1941) *Amer Heart J*, 21, 511
4. ALTSCHULE, *et al* (1940) *Amer J med Sci*, 200, 478
5. MILLER (1939) *Amer J med Sci*, 198, 323
6. NORMAN, ALLEN (1937) *Amer Heart J*., 13, 257.

The Circulation in Polycythæmia

Polycythæmia vera (Osler's disease) may be regarded as a primary type. The secondary varieties are met with in the cyanotic congenital lesions of the heart, and sometimes in mitral stenosis, emphysema, and after residence at high altitudes. A special type of polycythæmia vera has been associated with high blood pressure, Gaisbock's disease, or polycythæmia hypertonica.

It is in connection with polycythæmia vera that the adjustments of the circulation have been studied.

The great increase in the number of the red cells, which may reach thirteen million per c.m.m. increases the viscosity of the blood. This may be twelve or thirteen times as viscous as normal (1). The blood volume is also much increased; this is mainly due to the fact that the cell mass is two or three times above normal (2). The velocity of the blood flow from arm to tongue (decholin) is lowered (2). The slowing is also apparent at the periphery in the capillaries, for the arteriovenous oxygen difference is raised (3), and it can be seen that the capillary rate of flow is slowed in the large tortuous capillaries, where the red cells pass in wide columns instead of in single file (4).

Observations on the cardiac output have given conflicting results. Stewart and others (3) have found with acetylene, that the output is below normal for the patient. When the red count fell the output rose. It was thought that the lower output was compensatory for the abnormal state of the blood. It would explain why most cases have a normal blood pressure in spite of increased viscosity; it also tends to spare the heart needless work. In view of the high oxygen content of the blood, the tissues can do with a smaller output. On the other hand, Altschule (1), using ethyl iodide, found that the cardiac output at rest was normal. There was no slowing in the circulatory rate, and the venous pressure was normal. In some cases the vital capacity was low, but this may have been due to other causes.

Patients with this condition are prone to show the Raynaud phenomenon. Thrombosis is common, particularly in the cerebral arteries; a migrating type of thrombosis may be seen. Coronary occlusion is frequent. This may occur with minimal degrees of vascular disease (5). Occlusive vascular disease is also common

hearts vasa vasorum are only present in the adventitia of the coronary arteries, and the media is nourished from them, and from the blood in the main channel. But where an atheromatous plaque has formed and the intima is much thickened, new capillaries develop. These are usually derived from the vasa vasorum, but may grow in from the lumen of the vessel. The new capillaries are fragile and liable to rupture, and the artery then becomes narrowed by the resulting hæmatoma, or by the extrusion of the atheromatous plaque into the lumen through the pressure of the hæmatoma forming behind it A thrombus forms easily on the sticky surface of the protruding hæmatoma or atheromatous debris, and so secondary thrombosis completes the occlusion of the vessel. Of 37 cases with occlusion, 32 had an initial capillary hæmorrhage (4)

SITES OF INFARCTION. Myocardial infarcts are practically confined to the left ventricle, although a large infarct may extend across the septum to involve the right side as well. Infarcts are commonly found in two positions in about equal proportions: in the front of the left ventricle in the region of the apex, the *anterior infarct*, when the anterior descending branch of the left coronary is usually involved, and at the back of the left ventricle near the base, *the posterior infarct*, when either the right coronary or the circumflex branch of the left is affected. Sometimes occlusion of the latter artery gives rise to an infarct in the lateral wall of the left ventricle (*lateral infarct*) Infarcts may invade the septum interfering with conduction. A massive infarct may involve both anterior and posterior walls simultaneously.

Infarctions at a distance. When there has been progressive narrowing of one coronary artery, the collateral circulation may develop to such an extent that the muscle in the territory of the diseased artery may come [illegible]
narrowing of the ar[illegible]
the region at the a[illegible]
collaterals from the right coronary, and occlusion of this artery may then cause an anterior infarct.

Other Causes of Occlusion. CORONARY EMBOLISM. It is rare for an embolus, such as a fragment from a vegetation or intramural clot, to enter a coronary vessel and obstruct it (5). Thrombi round the aortic cusps in syphilitic aortitis have done so (6).

ACUTE MILIARY INFARCTION of the heart has been described

CHAPTER VII

CORONARY OCCLUSION, CORONARY INSUFFICIENCY, ANGINA PECTORIS

The association between Heberden's angina and cardiac infarction has long been recognised, but recent work has brought them so close together that they can now be considered a single chapter.

Sudden occlusion of a coronary artery causes cardiac infarction, but, if the process is gradual, the patient may suffer instead from angina pectoris. Cardiac infarction may also take place without a coronary vessel being occluded, if the work which the heart is called upon to do is out of proportion to the blood flow to the muscle (coronary insufficiency). Lastly, a diffuse myocardial fibrosis may arise as a result of the recurrent phases of ischæmia marked by attacks of angina of effort.

The Coronary Circulation

The coronary arteries vary in their size and distribution. In 40 per cent. the left coronary, dividing into the *anterior descending* and *circumflex* branches, supplies the left ventricle, while the *right coronary* supplies the right ventricle. In another 40 per cent the right coronary supplies also part of the left ventricle: while in the remaining 20 per cent a considerable part of the right ventricle is supplied by the left coronary. In this last group the incidence of occlusion is high, and infarcts often prove fatal (1). The coronary arteries are not, strictly speaking, end arteries, since fine communications up to 40μ in diameter exist between them in health (2). These collateral branches increase in size greatly when one of the main arteries is narrowed, so that much of its territory may come to be supplied by branches from the other.

Mechanism of Coronary Occlusion. Less than *one-third* of occlusions are due to a simple thrombosis (3). In the remainder the thrombosis is secondary to capillary hæmorrhage. In normal

HEALING OF INFARCTS. The time which an infarct takes to heal will depend upon its size. The necrotic muscle is replaced by connective tissue in fourteen days, but the formation of collagen which consolidates the scar does not occur until the third week. Small infarcts heal almost completely in a month. Large infarcts usually heal in two months, though islands of necrotic muscle may remain in the scar tissue (10) Extensive recanalisation of the thrombosed artery may take place.

Coronary Occlusion and Heberden's Angina. If the narrowing of the coronary artery has progressed slowly, the final occlusion may not result in an infarct. Such patients are likely to suffer from cardiac pain on exertion (13). In forty cases of Heberden's angina examined by Blumgart (2) occlusions or narrowing of the coronary arteries were found in all, and multiple occlusions in the majority. In some cases congestive heart failure followed a history of previous anginal attacks. In them, patchy myocardial fibrosis was evident, which differed in its distribution from that of an old infarct, and it seems that the transient ischæmia during an anginal attack may lead to fibrous scars in the muscle (1).

Cardiac Infarction

Predisposing Factors. *Age and Sex.* Men are more liable than women in the proportion of three to one (14). Most attacks occur between the ages of 45 and 65, but a series of fifty cases has recently been recorded in soldiers between the ages of 20 and 35, of whom 40 died (15).

Hypertension is present in more than half of all cases. A family history of coronary artery disease can be found in nearly one half.

Other Factors. An association with diabetes is present in 10 per cent Polycythæmia vera and polyarteritis nodosa may lead to coronary occlusion (16).

PRODROMAL ATTACKS. Preliminary attacks of substernal pain during the fortnight or so before the occlusion occur in about half of all cases. The attacks may simulate Heberden's angina although the pain may outlast the exertion Less frequently they occur at rest, lasting half-an-hour or more. They are uninfluenced by treatment, and no alteration in the electrocardiogram is found after the pain has subsided. These prodromal symptoms are probably related to the initial capillary hæmorrhages and

in patients with large hearts who have usually some superadded infection such as pneumonia or cystitis (7). The result is either sudden death, or urgent left ventricular failure.

CORONARY INSUFFICIENCY. Infarction without occlusion may occur in patients with large hearts in which the blood supply by reason of the hypertrophy is relatively insufficient. On exertion an area of the *myocardium may become ischæmic, and an infarct* may result. This is especially apt to happen in aortic stenosis where the aortic pressure is low (8). Other causes, associated with a fall in blood pressure, are severe hæmorrhage, post-operative shock, and prolonged tachycardia (9).

The Infarct. At first the muscle is rather pale and swollen: sometimes there are purple areas of hæmorrhage to be seen on the surface and round the edges. The small superficial vessels in the neighbourhood are engorged. Then the infarcted area becomes yellow-grey from leucocyte infiltration and loss of blood pigment; the border is reddish, owing to the presence of a zone of granulation tissue *consisting of newly-formed capillaries filled* with red cells (10). As time goes on, fibrous tissue infiltrates the infarct, surrounding the islands of necrosis, and the area becomes white.

The inner surface of the ventricle is usually more extensively involved than the outer, but a thin layer of muscle commonly survives immediately beneath the endocardium, being nourished either by the Thebesian veins, or directly from the blood in the ventricle. If the infarct reaches the pericardium, the *transmural infarct*, pericarditis results and adhesions, usually thin, may form; or merely an area of thickened epicardium results. On the inner surface of the infarct a mural thrombus may form: in one large series this was found in two-thirds of the cases (11). Mural thrombi begin to organize at the ninth day after infarction, and organization is complete by the sixteenth day (10).

CARDIAC RUPTURE. *Spontaneous rupture of the softened* area may occur, causing hæmopericardium and sudden death. Rupture of an infarct takes place most often during the first week. In one series of 70 cases, half had ruptured through the *anterior surface* of the left ventricle, and one-fifth through the septum (12). When the fibrous area is large, an aneurysm of the left ventricle may be produced, which may rupture months or years later. Occasionally the infarct becomes calcified.

and apathetic, but the mind is clear. These are signs of peripheral circulatory failure; but the venous pressure in infarction is normal or raised, and pulmonary congestion is invariable, and may sometimes reach a severe degree (21). Although the pulse pressure is small, the diastolic pressure is not so low as in pure peripheral failure, as a rule.

It is difficult to say how far the signs in the peripheral circulation are due to shock, or to gross deficiency in the output of the left ventricle. Acute left ventricular weakness with great diminution in cardiac output certainly plays a part.

Syncope. Especially in old people, a syncopal attack may mark the onset. The patient may be unconscious or semi-conscious, but convulsions do not occur (22). As consciousness returns, pain is felt. The cardiac rate is usually slow. *Vomiting* is almost invariable in this type. In other severe cases, also, vomiting may dominate the picture and mask other symptoms. Nausea is often present.

Blood Pressure. The blood pressure usually falls, and always does so if there is collapse. In patients with hypertension the systolic pressure may drop more than 100 mms. of mercury: the diastolic remains relatively high. In the early painful phase the blood pressure may rise temporarily (23).

Pulse. The pulse is not quickened unless shock is present, when it is small and weak. Acceleration above 100 beats per minute increases the gravity of the prognosis. In some cases the rate is rather slower than usual.

Physical Examination. Physical signs at the heart in the early stages are inconspicuous. The first sound at the apex may be weakened, and the sounds may be evenly spaced. A gallop rhythm may occasionally be detected, probably more often in hearts enlarged as the result of hypertension. The pulmonary second sound may be accentuated.

Pericarditis. Although localised pericarditis is common, pericardial friction is heard only in a small minority of cases and it is evanescent. When present, it is a valuable diagnostic sign. Localised pericarditis can only give rise to an audible friction in anterior infarcts, but in a small proportion of recent infarctions a general pericarditis was found (24), so that friction may on occasion be heard with a posterior infarct.

toma formation (17). They may begin on exertion and lead to a claim for compensation in industrial cases.

The Attack. Onset. Since in most cases the final occlusion is due to secondary thrombosis, exertion plays no part in determining the onset. Three-quarters of all attacks occur at night or during mild activity in the day (18). *Sudden death* may result when a large trunk is occluded, but death may also come suddenly to patients who have not rested at the onset because their infarcts caused no symptoms. Death here may be due to ventricular *fibrillation* (19) or *standstill* (20). Animal experiments suggest that the reflex coronary vaso-constriction may play a part. But the great majority of patients survive the onset, and experience a triad of symptoms, comprising pain, dyspnœa and collapse. In severe cases these are usually all present together in varying degree; in milder attacks collapse is commonly absent.

Pain. Pain is the most arresting symptom, and occurs in the large majority. The patient may experience anything from intense agony to a dull ache. The sensation is described as rending, tearing, or crushing. The site of the pain is usually substernal, and occasionally epigastric. From here it may radiate down the arms or up to the neck, jaws and teeth. Occasionally the pain starts at some other point such as the throat or back and spreads to the sternum later. With the intensity of the pain the patient cannot keep still; he may writhe in agony, or walk about. There is no relief in immobility, as in angina of effort. In milder cases the patient invariably says "I thought it was indigestion."

Duration. The pain may last from half-an-hour to several days, unless controlled by morphia. After the worst is over a dull ache may persist for a long time. Sometimes the pain is of the waxing and waning variety, causing successive attacks.

Dyspnœa. This is present in all severe attacks, though frequently masked by the pain. It is due to left ventricular failure which occasionally progresses rapidly to acute pulmonary œdema. beginning with a short dry cough. In fact, myocardial infarction should be suspected if a patient develops an attack of pulmonary œdema which cannot be explained satisfactorily on other grounds.

Collapse. In severe attacks the patient suffers from shock. He is both pale and cyanosed, with a greyish colour. The extremities are cold; profuse sweating is common. He is prostrate

Diagnosis

Recent Coronary Occlusion. CLINICAL. In most cases the diagnosis presents no difficulty. Prolonged substernal pain, accompanied by dyspnœa and collapse, with a fall in blood pressure, occurring in a patient with a history of recent anginal attacks, is unlikely to be due to anything but a cardiac infarct. It must be remembered that the attack may commence during exertion, but there is no relief in rest. Difficulties may arise when the attack is mild and the painful phase is not prolonged, or when the pain waxes and wanes, and the patient seems to have a succession of attacks of angina pectoris. Sudden dyspnœa with pulmonary congestion, or pulmonary œdema, may take the place of pain. Finally, the onset may be symptomless, or not remembered by the patient, who may come under observation for a complication such as cerebral embolism.

Changes in the Electrocardiogram. Changes in the electrocardiogram following myocardial infarction comprise the appearance of Q waves, elevation or depression of the RS-T junction, and inversion of the T wave.

Q Wave. Active muscle is electrically negative to inactive muscle. The impulse reaches the ventricles through the A-V bundle which runs in the subendocardial zone. It spreads almost at once to the ventricular cavities, which are therefore negative during the activation of the ventricular wall. As the impulse spreads outwards towards the epicardium, the charge on its advancing face will be positive. Since the electrical changes reach the surface of the body through the epicardium, and chiefly reflect the condition of the sub-epicardial muscle cells, the major initial deflection of a normal QRS is positive. If, however, the muscle cells have died as the result of infarction, there will be nothing to prevent the negative potential of the cavity reaching the surface. It is as if a window had been cut through the ventricular muscle (26). The initial deflection will then be negative, and deep Q or QS waves will appear. This will be seen best when the electrode is placed directly over the infarct as in precordial leads in anterior infarction.

RS-T Displacement. Surrounding the central core of dead muscle in an infarct, is a zone of muscle injured as the result of ischemia (27) In this area the state of excitation lasts longer

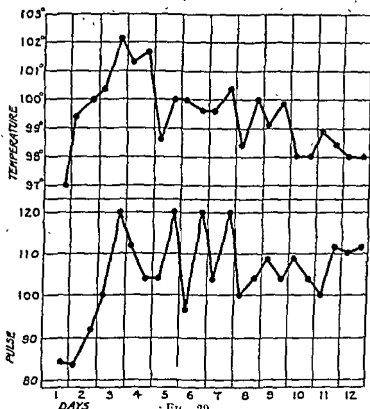


FIG. 29

Chart showing pulse and temperature in a man of 45 after myocardial infarction The attack began at 10 a m on the first day Note the sub-normal temperature at first, and the persistent tachycardia (Autopsy)

FEVER. After an initial phase when the temperature is subnormal, fever occurs in the majority of severe attacks at some time between the second and fifth day. The height of the temperature and the duration of the fever are useful guides as to the prognosis. Prolonged fever is rare, and is likely to be due to complications such as pneumonia.

LEUCOCYTOSIS. A moderate leucocytosis is common, commencing very soon after infarction. In uncomplicated cases the count does not usually rise above 15,000 per cmm.

THE BLOOD SEDIMENTATION RATE rises about the third day, and remains high for about a fortnight. It usually returns to normal by the end of a month (25). The B.S.R. is useful in distinguishing small infarcts from angina pectoris, but the height of the B.S.R. has little bearing on prognosis.

CHEST ELECTRODE. *Lead IV.* The precordial electrode is placed on the outer border of the apex beat as determined by palpation. If no apex impulse can be felt, the electrode may be placed in the fifth space just outside the left mid-clavicular line, if the outer border cannot be defined by percussion. The use of this lead has been largely superseded by that of multiple precordial leads.

MULTIPLE PRECORDIAL LEADS. The precordial electrode is placed on certain relatively fixed points on the chest, thus differing from lead IV, the position of which varies with the size of the heart. The points are numbered from one to six and are obtained as follows (32): The apex impulse is first located as in lead IV. In the first position the precordial electrode is placed on the *right* margin of the sternum in the fourth intercostal space; the second position is at the left margin of the sternum in the same space; the third is midway between the left margin of the sternum and the mid-clavicular line in the intercostal space in which lies the apex; the fourth is at the mid-clavicular line in this space; the fifth and sixth are at the anterior and mid-axillary lines at the same level. Thus the first two positions are fixed, while the remaining four vary in regard to their horizontal levels according to the space in which the apex lies. Multiple precordial leads are denoted by the letter "C", followed by a numeral showing the position of the chest electrode. Another letter is used for the distant, or indifferent, electrode.

INDIFFERENT ELECTRODE. Either the right arm (CR), the left arm (CL), or the left leg (CF), are available for the indifferent electrode, but CL leads are inferior and are not used. A recent comparison of CR, CF and CV leads in which the six chest positions were obtained by means of an elastic strap fastened across the chest, so that only the first and sixth positions were located accurately, showed comparatively little differences in the CR, CF, and CV curves (33). In fact CR and CF leads are sufficiently accurate in 90 per cent of cases, but in the remaining 10 per cent the error is appreciable (34). In CR leads the error is towards positivity, so that on occasion a T which should be negative may be positive in this lead. CF leads are almost completely accurate when the heart has a normal position or is semi-horizontal, and have only a small positive error when the heart is horizontal. (Left axis deviation.) When the heart is vertical (right axis deviation)

than normal. The current resulting therefrom in diastole is neutralised by the compensation current from the galvanometer during standardization. In systole the flow of the current of injury is reversed, and to it is added the current from the compensator on the galvanometer. The effect of the current of injury is, therefore, seen only in systole and causes displacement of the RS-T phase. If the injured zone extends to the epicardial surface, the displacement will be positive or upward in leads which face the advancing wave, such as precordial leads over an anterior infarct; it will be negative or downward, and of smaller amplitude, in leads which face the tail of the wave such as lead III in an anterior infarction. If the injured cells lie mainly in the subendocardial zone, *the displacement will be negative* (28). *Elevation of* the RS-T phase is also found in the early stages of diffuse pericarditis, since this involves the subepicardial muscle cells. As the injury in pericarditis is limited to the subepicardial zone, Q waves do not occur (Fig. 17).

Inversion of the T Wave. Inversion of the T wave is caused by changes which occur during the recession of the impulse, and indicates that the muscle is recovering imperfectly. A negative T occurs in many conditions associated with myocardial disease, but the inverted T of coronary occlusion has a characteristic shape. It is bowed or dome-shaped, and the inversion may at times be very deep. A negative T is the first change to be seen following the experimental occlusion of a coronary vessel, elevation of the RS-T junction comes later. After the release of the vessel the inversion of T is the last abnormality to disappear. The negative T is, therefore, associated with changes in the ischæmic muscle surrounding the infarct (29). In small subendocardial infarcts, due to coronary insufficiency, Q waves are absent, RS-T displacements may be slight and the bowed inversion of T may be the only definite sign of the infarct (30).

Precordial and Other Leads. In a joint memorandum issued by the British Cardiac Society and the American Heart Association (31), precordial leads have been standardized so that relative *positivity* at the precordial electrode is represented by an upward deflection of the galvanometer. For this purpose the left arm electrode from the machine is attached to the chest, and the right arm, or *left leg*, electrode is used as an indifferent or distant electrode.

CHEST ELECTRODE. *Lead IV.* The precordial electrode is placed on the outer border of the apex beat as determined by palpation. If no apex impulse can be felt, the electrode may be placed in the fifth space just outside the left mid-clavicular line, if the outer border cannot be defined by percussion The use of this lead has been largely superseded by that of multiple precordial leads.

MULTIPLE PRECORDIAL LEADS. The precordial electrode is placed on certain relatively fixed points on the chest, thus differing from lead IV, the position of which varies with the size of the heart. The points are numbered from one to six and are obtained as follows (32): The apex impulse is first located as in lead IV. In the first position the precordial electrode is placed on the right margin of the sternum in the fourth intercostal space; the second position is at the left margin of the sternum in the same space; the third is midway between the left margin of the sternum and the mid-clavicular line in the intercostal space in which lies the apex; the fourth is at the mid-clavicular line in this space; the fifth and sixth are at the anterior and mid-axillary lines at the same level. Thus the first two positions are fixed, while the remaining four vary in regard to their horizontal levels according to the space in which the apex lies. Multiple precordial leads are denoted by the letter "C", followed by a numeral showing the position of the chest electrode Another letter is used for the distant, or indifferent, electrode.

INDIFFERENT ELECTRODE. Either the right arm (CR), the left arm (CL), or the left leg (CF), are available for the indifferent electrode, but CL leads are inferior and are not used. A recent comparison of CR, CF and CV leads in which the six chest positions were obtained by means of an elastic strap fastened across the chest, so that only the first and sixth positions were located accurately, showed comparatively little differences in the CR, CF, and CV curves (33). In fact CR and CF leads are sufficiently accurate in 90 per cent of cases, but in the remaining 10 per cent the error is appreciable (34) In CR leads the error is towards positivity, so that on occasion a T which should be negative may be positive in this lead. CF leads are almost completely accurate when the heart has a normal position or is semi-horizontal, and have only a small positive error when the heart is horizontal. (Left axis deviation.) When the heart is vertical (right axis deviation)

there is a fairly considerable error towards the negative, and inverted T waves may be found in the absence of heart disease. To obviate these difficulties Wilson (26) devised the technique of the CV leads.

V LEADS. The standard leads are bipolar; lead I expresses the algebraic difference between the potentials obtaining at the right and left arm. In the case of precordial leads the effect of the distant electrode is slight compared with the electrode on the chest, but is not negligible (p. 000). Einthoven postulated that the algebraic summation of the potentials at all three points on his triangle at any given moment in the cardiac cycle is zero. Wilson used as the distant electrode all the three limbs connected through resistance *of 5,000 ohms to a central terminal. These leads are termed "V"* leads (32). Goldberger (35) simplified the technique when he found that identical curves could be obtained without the central resistance. To obtain "V" leads by his method it is only necessary to attach the right arm lead from the galvanometer to a central terminal from which issues three leads which are connected to the limbs. The same six points on the chest are used as in CR or CF leads and they are numbered V1-V6. The validity of the Einthoven triangle hypothesis, and therefore of this method of obtaining *unipolar leads,* has been contested by *Wolferth (36), but his* grounds do not seem very convincing.

UNIPOLAR LIMB LEADS. By a slight modification of the same technique the potential variations at the three limbs can be recorded separately. The left arm electrode from the galvanometer is attached to the limb to be examined, while two of the leads from the central terminal are attached to the other two limbs. The third is allowed to hang loose (37). These leads are named VR, VL, VF (p. 418). Formerly all three limbs were attached as in the case of *precordial leads, and a second electrode was tied to* the limb to be examined. But the deflections by this method were small and not easily read. By the newer method the deflections are increased by 50 per cent and can be more easily measured. Since the left arm faces the left ventricle the changes of anterior infarction will be reflected in the left arm lead (VL). The left leg faces the diaphragmatic surface of the heart and the changes of posterior infarction will be reflected in the left leg lead (VF).

The complete electrocardiographic investigation therefore

requires at least 12 leads and the procedure is somewhat laborious. For clinical purposes we have found that the standard leads and three chest leads give all the information ordinarily required. For infarcts V2 and two leads bracketing the apex are suitable. For right bundle branch block and right ventricular hypertrophy, it is better to use V1, since it is on this lead that in these conditions the diagnosis chiefly rests (p 000).

ŒSOPHAGEAL LEADS. If the patient swallows a flexible tube containing an electrode, deflections may be obtained when the tube reaches the level of the heart. The pharynx must be anæsthetised for this procedure. Records have been obtained with a Ryle's tube which can be passed along the nares (38), but we have been unable to obtain good contact with it. At 15-53 mm. distance from the teeth the electrode will be opposite the ventricles. In posterior infarction the œsophageal electrode faces directly the spread of the impulse and deep Q waves with elevation of the RS-T junction followed by a negative T will be found, as in precordial leads after an anterior infarct (39).

Anterior Infarction. Following an anterior infarct deep Q or QS waves appear in the precordial leads and to a lesser degree in lead I and VL, and the RS-T junction is elevated above the base line. In lead III the RS-T junction may be depressed although this feature is not necessary for diagnosis (Fig. 30). These abnormalities last for some hours to some days. Then the raised RS-T junction in the precordial leads, lead I and VL becomes

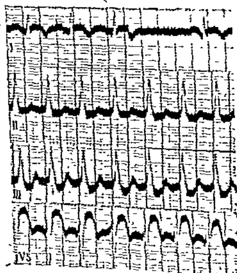


FIG 30
Anterior infarction with nodal tachycardia Note end of paroxysm in lead I

iso-electric and T is inverted. The coronary T wave has a peculiar dome shape on the down stroke and the inversion is sharply pointed and in the precordial leads may be very deep. The depressed RS-T in lead III disappears and the T wave becomes positive with a sharp point. The inverted coronary T tends gradually to return to the normal; the Q wave, especially in the precordial leads, often persists. The abnormal features differ somewhat in antero-septal and antero-lateral infarction.

Antero-Septal Infarct. In this type the standard leads may be normal. But in V1, V2, V3, and V4 deep QS waves appear with

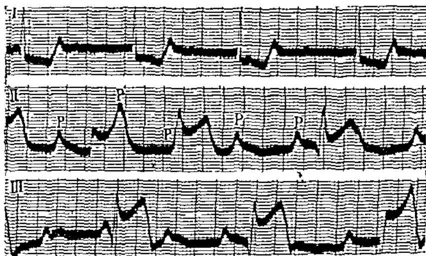


FIG 31

Coronary occlusion with posterior infarction and complete heart block. The right coronary artery was blocked by an embolus at its orifice.

elevation of the RS-T junction, followed by a negative T, which is most conspicuous in V3 and V4. V5 and V6 are relatively normal.

Antero-Lateral Infarct. The changes here are reflected to the left arm and are therefore obvious in leads I and VL. Precordial leads show the clearest abnormalities in V4 and V5.

Posterior Infarction. In this type the same distinctive features are seen in lead III, in VF, and to a less extent in lead II, as occur in the precordial leads and lead I in anterior infarction. There is elevation of the RS-T junction and Q waves appear (Fig. 31). A negative T wave in due course takes the place of the raised RS-T junction. There may be depression of the S-T

phase in lead I and in the chest leads in the early stages. Œsophageal leads taken from the ventricular level show changes similar to those in precordial leads in anterior infarction.

A small Q and inverted T in lead III are sometimes seen in obese persons with horizontally placed hearts, although lead II in this type is always normal (41).

In those in whom Q_3 is due to coronary disease, there is often a small Q and a flattened T in lead II A Q in lead III is of increased significance if S is absent in lead I (40) Lead VF is also useful in distinguishing those due to a horizontal heart and those due to previous infarction (41). In horizontal hearts S waves are present in this lead preceded by a definite R. In nearly all cases who had had previous posterior infarcts Q waves were seen in VF, the voltage being more than in one quarter of the R waves The exceptions were infarcts located high on the posterior wall: in them lead VF was normal.

Lateral Infarcts. Infarctions confined to the lateral wall of the ventricle are uncommon. In some instances a different kind of electrocardiogram is found. The T wave is inverted in leads I and II and an S wave may appear in lead III (42). The RS-T junction in the precordial lead near the apex is deeply depressed.



FIG 32

Infarction of lateral wall There is depression of S-T interval in leads I and II and deep depression of ST junction in V3 and V4 Auricular premature systoles are present in leads I and II

These changes may last a short time only and they resemble those found in digitalis saturation (Fig. 32) Before they can be accepted as indicating infarction it must be ascertained that the patient has had no digitalis for the preceding fortnight. Four cases out of nine with lateral infarcts verified at autopsy had electro-

cardiograms of this type. Others had curves of anterior or posterior infarction (43). There is also a tendency for auricular fibrillation to occur more frequently as a complication in lateral infarction than in infarction at the more common sites.

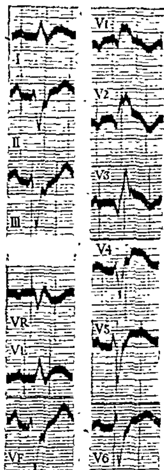


Fig 33A

Anterior infarct with right branch block Note presence of Q wave in V1, V2 and V3, with bowed inversion of T in V1, V2, V3 and V4 The intrinsic deflection is delayed on the right side by 0.14 second and is early on the left Autopsy showed an anterior infarct involving the septum

In some cases of lateral infarction where the precordial leads were normal, Q waves and negative T waves were seen when leads were taken across the chest at the level of the second or third intercostal space, ending high up in the left axilla This

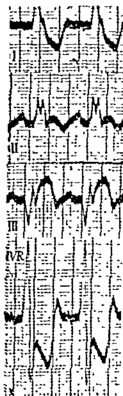


Fig 33B

Posterior infarct with left bundle branch block.

procedure is suggested when lead I and VL are typical of infarct, but the usual chest leads are normal (44).

Septal Infarcts. The interventricular septum is involved in 15 per cent of all infarcts, and, conversely, coronary occlusion is not an uncommon cause of bundle branch block (45). If the whole of the septum is involved, from front to back, signs of antero-septal infarction will be present in chest leads, while standard leads will show posterior infarction (45a). In most cases the electrocardiogram shows A-V heart block or bundle branch block.

If the right branch is involved, Q waves appear in leads to the right of the precordium (V1, V2, V3), the QRS is prolonged, and a bowed coronary T wave comes off from the descending limb of the broad R (Fig. 33A). This combination is not uncommon. In posterior infarction bowed T waves may be seen in leads II and III. In the case of left bundle branch block the large broad complexes usually engulf the RS-T displacement and negative T waves of infarction, though some curves show them (Fig. 33B). Also the left ventricular cavity is positive in left branch block until the impulse has crossed the septum and this prevents the occurrence of Q waves. Only if the infarct has involved the whole thickness of the septum will the negative potentials from the right ventricle be transmitted through it at once and allow Q waves to appear. Otherwise the presence of a left bundle branch block *precludes* the diagnosis from the electrocardiogram of anterior or posterior infarction (26).

Auricular Infarcts. Infarction of the auricles may occur. The P waves are dome-shaped or negative and there is also depression of the P-Q interval (46). Many of these cases show abnormal rhythms such as auricular fibrillation or flutter, or auricular premature beats (47).

Successive Infarcts may each leave their impress upon the curve but do not usually cause difficulty in diagnosis.

Effect of Pericarditis. Early *diffuse* pericarditis causes elevation in the RS-T junction in about *half* of those in whom it is diagnosed clinically (48) (p. 87). Since the injury is limited to the subepicardial zone Q waves are not found. The raised RS-T is usually present in all leads (49), but may occur in leads I and II only (50). Later the T wave becomes negative in all leads (51).

Localized pericarditis ...

cardiographic changes due to the infarct. The elevation of the RS-T junction in diffuse pericarditis may obscure temporarily the RS-T *depression of a posterior infarct in lead I* and the precordial leads, or that of an anterior infarct in lead III and the œsophageal leads, but this is not of much importance.

Muscle Bundle Localization. It should be mentioned that a series of articles have appeared (52, 53) suggesting localization by the muscle bundles, of which there are four. The picture of an anterior infarct might be given by a lesion of the deep sino-spiral muscle, that of a posterior infarct by involvement of the superficial *bulbo-spiral muscle*. Destruction of the superficial sino-spiral caused elevation of the RS-T junction with inversion of T in all leads, while it is suggested that infarction of the deep bulbo-spiral would cause elevation of the RS-T junction with upright T waves in all leads. This work lacks confirmation from other sources. Too little is known about the function of the muscle bundles to draw any conclusions.

Summary of Electrocardiographic Changes. The association of deep Q waves in the appropriate leads, with displacement of the RS-T junction, followed by inversion of the T wave, which is found when a major artery is occluded, and the whole thickness of the ventricular wall is affected, is pathognomonic. In one series the electrocardiographic findings both as regards the presence of a recent acute infarct, and the localization, were confirmed at autopsy in every case (54). There was rather less accuracy in localization when the infarcts were multiple The onset of characteristic changes may be delayed for twenty-four hours (55).

In small infarcts, involving only the sub-endocardial zone, such as occur in coronary insufficiency, Q waves are absent. Displacements of the RS-T phase may be slight and reliance must be placed on the presence of bowed "coronary" T waves. In cases of this sort multiple precordial leads are especially valuable. Such appearances in both V3 and V4 are practically confined to infarcts and pericarditis, *and pericarditis can usually be distinguished* clinically. An infarct in an unusual site may cause difficulty; *a negative* T wave in all limb leads, suggesting pericarditis, was found in one case involving the right ventricle (56). *Where the* diagnosis is in doubt serial electrocardiograms should be taken,

since successive changes in the curve form the firmest basis for diagnosis.

Diagnosis of Previous Infarction. The diagnosis of previous infarction can often be made from the history. It may be suspected if a patient with a normal blood pressure has congestive failure with enlargement of the heart, and no other cause can be found. Confirmation may be sought in certain changes in the electrocardiogram and in the contour of the heart on cardioscopy. Although the changes due to a lateral infarct may not last long, the Q wave in the precordial leads of an anterior infarction seldom returns to normal (57). The finding of a deep Q in the precordial leads to the left, at any time, strongly suggest a previous anterior infarction; an R wave of less than 2 mms. is also significant. A small Q deflection in V4 or 5 is common in left-sided hypertrophy; it may occasionally be seen in displacement of the heart, and removal of a left pleural effusion caused the reappearance of an R in CF 4 (58).

Radiological Appearances. Since the patient has to stand for these procedures, cardioscopy should not be employed in recent infarction. Pulsation at the apex, or just above it, is reversed with a localized outward expansion during systole. A double pulsation or delayed pulsation may also be seen (59) The antero-posterior position is best for anterior infarcts and also furnishes information in some posterior infarcts (60), in others the left oblique is better. *Pulsation* may be absent or diminished in the area involved, but diminished pulsation is also *found* in cardiac failure with gross enlargement of the heart (61), Pick's disease, and in pericardial effusion, whilst local reversal of pulsation, *or* systolic expansion, is only seen with infarction.

These features *do* not usually appear until after the second week (62), but they *have* been noted on the day after infarction (59) They may persist for *years*; but they have gone in a year in about half of the cases, and their disappearance, or change to diminished movement, signifies an improved prognosis. The recovery rate was higher in those *who* did not show reversed pulsation and very few of those *in* whom the abnormalities persisted made good recoveries (61).

Kymograms allow the pulsations to be recorded by means of a multiple slit grid, and measured on a film. Abnormal [illegible]

were recorded in nearly all cases of infarction (63). The site of abnormal pulsation agreed with electrocardiograms in three-quarters of them (64).

Differential Diagnosis. It should be emphasized that none of the other conditions giving rise to *prolonged* substernal or epigastric pain is associated with the electrocardiographic changes of cardiac infarction, except very rare cases of dissecting aneurysm involving a coronary artery. A typical electrocardiogram almost always establishes the diagnosis.

Acute Abdominal Disease. Pain in the epigastrium may resemble an acute abdominal emergency such as a perforated peptic ulcer, gall stone colic, or acute pancreatitis. Infarction may follow a severe hæmatemesis, and rarely an infarct and an acute ulcer or acute cholecystitis may develop simultaneously (65).

In the absence of an electrocardiogram, the following points will suggest infarction.

1. A history of previous attacks of substernal pain on exertion.
2. The presence of dyspnœa, without the pain of pleurisy.
3. Evidence of pericarditis, or of pulmonary congestion.
4. The pain almost always tends to spread upwards.
5. Absence of tenderness and of the rigidity of peritonitis.

Pneumothorax or Pneumomediastinum cause pain, dyspnœa and shock. In pneumomediastinum the pain may be substernal. A small left-sided pneumothorax can cause pain in the left upper chest which may persist for days. A systolic click may be found which the patient can hear himself (66). In mediastinal emphysema peculiar crackling sounds like those of surgical emphysema—they change with the heartbeat and breathing—are audible over the precordium. The T wave may be inverted in leads II and III or chest leads (67). All these conditions tend to occur in younger age groups than infarction.

Dissecting Aneurysm may be difficult to distinguish in the early stages. The signs and symptoms are discussed on page 390.

An Œsophageal Pouch may give rise to substernal pain through the effect of distension of the œsophagus, and the pain may last an hour or more.

Complications. About three-quarters of the patients, if kept in bed, will make a straightforward recovery. Of the complications

that occur in the remainder, most may be expected during the first fortnight.

Death may take place from *ventricular fibrillation* (68), or from a reflex coronary spasm while pain is still present.

Pulmonary Œdema is the most common complication, as might be expected in a condition affecting almost exclusively the left ventricle. About half of these die when this develops.

Hypostatic Pneumonia may be the consequence of severe pulmonary congestion aided by the immobility of the patient. The signs are prolonged fever, increase in respiratory rate, tachycardia, cough with purulent sputum, and consolidation at the bases.

Congestive Heart Failure may supervene with venous engorgement and œdema This is most likely to occur in patients who have had previous infarcts, or whose hearts are enlarged from hypertension.

Cardiac Rupture During the first few days recurrent attacks of angina at rest accompanied by pulmonary congestion may signify weakening of the ventricular wall, and death may occur from cardiac rupture with hæmopericardium We have seen it within twelve hours of the onset of infarction. As a rule death is almost instantaneous, but there may be time for tamponade to develop, with signs of venous engorgement, cyanosis, and respiratory embarrassment, which soon proves fatal

Perforation of the interventricular septum may take place, either in anterior (69) or posterior infarction (70), usually in those who do not rest immediately after the occlusion. Precordial pain and shock may come on, and the rough systolic murmur of a ventricular septal defect is heard with a systolic thrill. Intractable failure of the right ventricle then results in consequence of the shunt from left to right (71) One patient survived the perforation for five years with persistent œdema throughout (70). If an aneurysm of the septum forms first, the signs of subsequent rupture are less conspicuous, and the development of a systolic murmur may be the only clue (72).

DISTURBANCES IN RHYTHM. *Auricular Fibrillation* is uncommon Paroxysms usually begin during the first week. Lateral infarcts have a tendency to be accompanied by fibrillation (43), or the auricles may be involved in the infarction (17). In

some severe attacks, fibrillation commencing near the onset, increases the gravity of the prognosis. Nearly all of the patients die in whom fibrillation persisted more than a day (73). In others, who may have suffered from paroxysms before, or have a mild form of rheumatic heart disease, the paroxysms are of little importance and do not last long. Auricular flutter and paroxysmal auricular tachycardia may occur (Fig. 30), and recovery has been recorded with ventricular rates of over 300 (74) Nodal rhythm is said to have a bad prognosis (75).

Ventricular Tachycardia is a serious complication which is likely to prove fatal unless it responds to prompt and effective treatment with quinidine (p. 300). But is is rarely found unless digitalis has been given. The frequent appearance of *Ventricular Premature Beats*, particularly when they arise from numerous foci, may be a precursor of ventricular tachycardia (76).

A-V Heart Block. Apart from some prolongation of the P-R interval, which does not influence prognosis, heart block occurs in 8 per cent only (77). A posterior infarct is usually present, and complete heart block comes on from the first to the fifth day (Fig. 31). The prognosis is usually bad : the patient may develop Stoke-Adams attacks, or collapse owing to the greatly diminished cardiac output due to the combination of the slow rate and low blood pressure, but sometimes the block clears up.

EMBOLISM Embolism is most likely to occur during the first ten days. Patient with large infarcts are mostly affected, as endocardial thrombosis is found in half of those who die. In a series of 160 autopsies, emboli were found in one or more arteries in nearly half, and the embolus was the main cause of death in a quarter (78). The embolus may lodge in a cerebral vessel or block a peripheral artery. An unexplained hemiplegia may be due to cerebral embolism from a coronary occlusion. But hemiplegia, convulsions and coma may also occur in patients with advanced cerebral arteriosclerosis in the absence of emboli, and are due to the impairment of the cerebral circulation consequent upon the diminished cardiac output (79). There may be a primary cerebral thrombosis from the same reason.

Pulmonary emboli are the most common ; they may come later from a primary thrombosis in the veins of the leg, a possibility which is favoured by the immobility of the patient (76). Or further

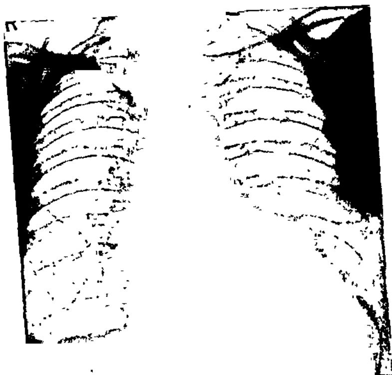


Plate 24

Aneurysm of the Left Ventricle.



PLATE 25

Aneurysm of the Left Ventricle.

Oblique view of case shown in Plate 24.

thrombosis may occur in the left ventricle as the result of congestive failure and lead to emboli in the systemic system (16).

Patients with cerebral emboli from intraventricular thrombosis often do surprisingly well and recover without any residual palsy. Embolism of a peripheral artery following coronary occlusion is a disaster The patient is not in a condition to stand embolectomy and one can only try to re-establish the circulation with intravenous papaverine and heparin. The use of dicoumarol promises well (p. 213).

Among the later sequelæ of infarction are the development of a *cardiac aneurysm* and *left shoulder pain*.

Cardiac Aneurysm. If an infarct has involved the whole thickness of the ventricular wall, local weakening may lead to the formation of a cardiac aneurysm. They seem to occur especially in those who rested a few days only during the acute phase (60). The aneurysm is usually situated at the apex or anterior wall of the left ventricle. The diagnosis can be made clinically by a diffuse pulsation over a wide area of the precordium extending upwards two or more spaces from the apex, and inwards almost to the left sternal border (81). The pulsation is expansile, and separate from the actual apex thrust. On X-ray examination the left border of the heart assumes a somewhat rectangular appearance. A localized bulge may be found on the left border (Plate 24), and calcification may be visible within it. In the right oblique position the aneurysm may project as a flat ledge towards the back of the sternum (Plate 25) (82). The sac may show expansile pulsation, or none at all (83). The prognosis is fair and considerable activity is possible. Patients usually die from congestive failure or from repeated emboli due to thrombosis in the sac. In one series there was no case of rupture (84).

Left Shoulder Pain. A curious condition of pain, with limitation of movement, at the shoulder may develop in the months following infarction The left shoulder is affected more than the right, but both may be involved together ... disability simul...
history of so...
pain in the ...
and early D...
unknown ... may be present. The cause is

ischaemia combined with a pre-existing affection of the shoulder seems most likely. A gouty origin has been suggested (88). Relief can sometimes be obtained by massage, or by firm pressure under evipan on tender points along the upper border of the scapula.

Treatment. The treatment of infarction aims at reducing the work of the heart to a minimum during the critical phase immediately after infarction, and increasing by all possible means the collateral circulation.

Morphia. Morphia should be given at once, as the sooner the pain is controlled, the less likely is the patient to die from syncope. The intravenous route gives most rapid relief and is safe. Morphia, gr. 1/6 intravenously, and gr. $\frac{1}{4}$ subcutaneously, should be given, followed by further doses of gr. $\frac{1}{4}$ subcutaneously, as required.

Rest in Bed. It is essential that patients should be kept strictly at rest in bed. In severe attacks this is obvious, but minor attacks may be missed. These patients are more likely to develop post-infarction angina or cardiac aneurysm. The patient is kept in bed for an average period of four weeks. With small infarcts affecting only the sub-endocardial zone, who show no Q waves, less time may be needed because they heal more quickly. On the other hand in large infarcts where the patient is collapsed at the onset, where fever is prominent and the pulse rate exceeds 100, and when pulmonary congestion and other complications, including pericarditis, develop, rest in bed up to two months may be necessary.

Oxygen. Oxygen therapy is valuable if cyanosis develops at any stage, and also if pain persists, or recurs, in spite of adequate doses of morphia at the onset. If available, an oxygen tent is the most satisfactory method, preferably the small open top type in which the patient is not cut off from sound. Otherwise a B.L.B. mask, or nasal catheter, can be used.

Coronary Dilators. Experimentally it has been shown that theobromine sodium acetate, cardophylin, and atropine given promptly reduce the mortality rate in dogs by one half (89). Clinically cardophylin 0.24 gm. in 10 cc. given intravenously may tide the patient over a crisis such as the development of heart block or auricular fibrillation, or it can be administered with the morphia at the onset in severe cases. We have found it both safe and effective to use the ampoules containing 0.48 gm. in 2 cc.

intravenously in these cases providing the injection is made slowly.

THE ALIMENTARY SYSTEM. In severe cases, or when vomiting is present, only drinks sweetened with glucose to combat acidosis should be given for some days. Full doses of atropine may control vomiting. During this time the bowels should be left alone. If a natural action has not taken place, an enema can be given later. A low diet containing 800 calories has been recommended during the whole period of rest in bed on the ground that such a diet reduces the basal metabolic rate, and so the pulse rate (90). This diet is rather severe, but patients tolerate a diet consisting of carbohydrate, 100 gms., protein 45 gms., fats 35 gms., with a total caloric value of 900. On this diet thin patients maintain their weight at rest, while stout patients reduce their bulk, which is to their advantage.

DIGITALIS should be used with great caution because of the risk of provoking ventricular tachycardia. It should not be given at all unless venous congestion and œdema appear; and even then it is better to try first the effect of the mercurial diuretics, oxygen, venesection, and coronary dilators (90). Should these fail, digitalis should be given in full doses by the *intravenous* route (see p. 347).

QUINIDINE should be given at once to stop the dangerous *complication* of ventricular tachycardia (see p. 300). Large doses may be required, and an intravenous injection may be most effective. In the case of auricular fibrillation, it is well to remember that the drug is depressing and inadvisable *in the presence* of congestion. It may be better to withhold quinidine for some hours as the [illegible]

I [illegible]

in c[illegible]

ant[illegible] which is effective when given by mouth. Dicoumarol is supplied in 50 *mg.* tablets.

Action. Dicoumarol increases the prothrombin time, which is the time that a preparation of thrombokinase takes to coagulate the plasma of the patient. The dosage of dicoumarol is controlled by observing its effect upon the amount of *prothrombin* present in the blood. Since direct chemical measurement of the prothrombin is impossible, indirect meth[illegible]

ischæmia combined with a pre-existing affection of the shoulder seems most likely. A gouty origin has been suggested (88). Relief can sometimes be obtained by massage, or by firm pressure under evipan on tender points along the upper border of the scapula.

Treatment. The treatment of infarction aims at reducing the work of the heart to a minimum during the critical phase immediately after infarction, and increasing by all possible means the collateral circulation.

Morphia. Morphia should be given at once, as the sooner the pain is controlled, the less likely is the patient *to die from syncope.* The intravenous route gives most rapid relief and is safe. Morphia, gr. 1/6 intravenously, and gr. ¼ subcutaneously, should be given, *followed by further doses of gr. ¼ subcutaneously, as required.*

Rest in Bed. It is essential that patients should be kept strictly at rest in bed. In severe attacks this is obvious, but minor attacks may be *missed*. These patients are more likely to develop post-infarction angina or cardiac aneurysm. The patient is kept in bed for an average period of four weeks. With small infarcts affecting only the sub-endocardial zone, who show no Q waves, less time may be needed because they heal more quickly. On the other hand in large infarcts where the patient is collapsed at the onset, where fever is prominent and the pulse rate exceeds 100, and when pulmonary congestion and other complications, including pericarditis, develop, rest in bed up to two months may be necessary.

Oxygen. Oxygen therapy is valuable if cyanosis develops at any stage, and also if pain persists, or recurs, in spite of adequate doses of morphia at the onset. If available, an oxygen tent is the most satisfactory method, preferably the small open top type in which the patient is not cut off from sound. Otherwise a B.L.B. mask, or nasal catheter, can be used

Coronary Dilators. Experimentally it has been shown that theobromine sodium acetate, cardophylin, and atropine given promptly reduce the mortality rate in dogs by one half (89). Clinically cardophylin 0.24 gm. in 10 cc. given intravenously may *tide* the patient over a crisis such as the development of heart block or auricular fibrillation, or it can be administered with the morphia at the onset in severe cases. We have found it both safe and effective to use the ampoules containing 0.48 gm. in 2 cc.

Five patients received an average of 600 mg. weekly for more than two years During this time they remained free from attacks although they had each had three in the year before treatment was begun. The prothrombin time was estimated daily for the first few weeks and later every fortnight. No toxic reactions were observed (98)

Toxic Reactions. In overdosage, there may be generalized bleeding into the skin, from the nose, intestine, and kidney, or into the brain. The hæmorrhages may be fatal and may occur at the time when the prothrombin index is but little decreased. Dicoumarol should not be given to any patient with renal or hepatic disease, or any blood disease associated with purpura. In cases of cardiac infarction, hæmorrhages have been either slight (97) or absent (95).

Results. Vascular complications have been considerably reduced by the administration of dicoumarol; in one series of 50 cases from 16 per cent to 2 per cent (94), in another from 37 per cent to 4 per cent (97). Dicoumarol, therefore, lessens the risk of emboli, but the dangers attending its use make it unsuitable unless the prothrombin content of the blood can be estimated daily.

After Care. A prolonged convalescence is necessary after infarction in order to allow the collateral circulation to develop and the rest of the myocardium to adjust itself. Even with a small infarct and without complications, the patient should wait three months before resuming his work. Large infarcts require longer. A further slow improvement may then be expected which will continue until a year has elapsed.

Prognosis. The mortality rates in the first attack vary from one-tenth in a general series (90) to one-third among patients admitted to hospital (75), which would not include the milder attacks. Of those who survive this attack by three months, rather less than half live for more than ten years (99). The total average expectation of life is three and a half years (100).

A return to active life is often possible. Favourable factors are the absence of cardiac enlargement due to hypertension, or diffuse coronary artery disease. The risk of successive attacks cannot be assessed, but they are common, and the patient may survive three or four, dying finally in congestive failure.

The prothrombin time (91) is the rate at which plasma is clotted by a solution in which prothrombin is the only variable. The normal time is about 12 seconds. Different sources of thrombokinase—either from brain extract or snake venom—give different figures for the normal. *The prothrombin index* (92) avoids this difficulty by expressing the time as a percentage of the normal time for the thrombokinase used. *The prothrombin concentration* (93) is calculated from the prothrombin time by means of a table and expresses the actual amount of prothrombin present as a percentage of the normal. The confusion arising from these different methods is increased by the fact that some workers use a diluted serum which gives another set of figures again (94). The prothrombin index, with undiluted blood, is probably the best method to use.

The aim of treatment is to decrease the prothrombin index to the neighbourhood of 50 per cent. This corresponds to a prothrombin time of 30 seconds, or a concentration of 23 per cent At this level it is claimed that no fresh thrombi will form, nor will accretions be added to existing thrombi. It is the fresh clots which are friable and liable to become detached (95). If the prothrombin index falls below 40 per cent, hæmorrhages may occur, but they can usually be controlled by the combined use of intravenous vitamine K (menadione bisulphite) 50-60 mg. and transfusions of blood (96).

Administration. 300 mg. is given on the first day and 200 mg. subsequently. The prothrombin index is estimated daily, and the dicoumarol is omitted on any day on which the index is below 50 per cent. The drug is continued until all risk of emboli seems to be passed; the average length of treatment in one series was 24 days (97). In urgent cases, such as embolism of the femoral artery, an initial dose of 150 mg. of *heparin* should be given intramuscularly at once. This is followed by 75 mg. every six hours for the forty-eight hours that elapse before dicoumarol becomes effective.

Indications. Dicoumarol therapy should be begun at the first sign of embolism or of extension of the coronary thrombus. It should also be considered in all severe cases where it seems likely that clots may be forming in the ventricles. Dicoumarol has been given over long periods to prevent recurring attacks of infarction.

negative or the complexes of bundle branch block may appear transiently (104). A decrease in amplitude of the T wave, it must be remembered, may occur in normal subjects after exercise (105). An anoxæmia test has been devised, in which the patient breathes at atmosphere of 10 per cent oxygen and 90 per cent of nitrogen. The test continues for twenty minutes unless pain comes on earlier. Pure oxygen is then substituted (106). An abnormal response, found in half the cases, consists either of a combined RS-T displacement in the standard leads, and in IV F, of not less than 3 mms.: or of partial or complete reversal of T in lead I, coupled with an RS-T displacement of 1 mm. in that lead: or complete reversal of T in lead IV F (107).

A significant proportion of cases had very unpleasant reactions such as pulmonary œdema, convulsions, mental confusion or vaso-vagal attacks (108), so that these tests appear to be too risky and complicated for ordinary clinical use.

AORTIC DISEASE. *In Syphilitic Aortitis* proliferation of the intima round the mouths of the coronary arteries may occlude them almost completely. If aortic regurgitation is present as well, the mean arterial pressure is low, and the heart will be hypertrophied There is then a combination of diminished blood supply and an overworked overgrown muscle.

Aortic Stenosis leads to a gross hypertrophy of the left ventricle. In grossly hypertrophied hearts the new capillary formation may not keep pace with the hypertrophy of the muscle fibres, so that the cells are poorly nourished. Their increase in diameter makes the diffusion of oxygen through their substances difficult. The rigidity of the valves interferes with the filling of the coronary circulation in addition the systolic pressure is low. Angina is common in old men with advanced aortic stenosis due to the fibrocalcareous degeneration of Mönckeberg

Rheumatic Aortic Incompetence. Occasionally in young people with free aortic regurgitation of rheumatic origin attacks of cardiac pain occur at rest (109) The attacks are caused by emotion in individuals with unstable vasomotor systems. The blood pressure rises considerably during the attack; and the heart rate increases The tachycardia is probably of more importance in producing pain than the rise in pressure. Amyl nitrite gives quick relief. [illegible]

Angina Pectoris

Herberden, in 1768, first described a "disorder of the heart," "marked with strong and peculiar symptoms, considerable for the kind of *danger belonging to it*." Parry wrote in 1799, following a suggestion of Jenner: "The rigidity of the coronary arteries may act, proportionably to the extent of the ossification, as a mechanical impediment to the free motion of the heart; and though a quantity of blood may circulate through these arteries . . . yet there may probably be less than what is requisite for ready and vigorous action." Recent work has done much to prove the truth of these older observations. Herberden's angina is due to a transient relative anoxæmia of the myocardium, and all attacks are attended by a possibility of sudden death.

Incidence and Aetiology. SEX AND AGE. Three-fourths of the cases are over fifty, and the ratio of males to females is 3 to 1 (101).

Coronary Artery Disease. Many patients with angina pectoris have advanced atheroma of the coronary arteries. If the narrowing has progressed slowly, the development of a collateral circulation may be sufficient to prevent infarction when the final occlusion occurs. Two or three coronary branches may be occluded in such cases (1). *Anginal attacks may appear first after infarction,* particularly if the patient has not been kept at rest.

Electrocardiograms. BETWEEN ATTACKS. Abnormal electrocardiograms were found in two-thirds of the cases in one series (102). Among the most common changes are those indicating a previous infarction. Thus Q waves or pointed inversion of T may be present in lead III or VF or in one or more precordial leads. The presence of myocardial disease may be shown by a bundle branch block, or latent heart block, by a low voltage curve, or by notching of the QRS. In fact, any abnormality affecting the ventricular complex supports *the diagnosis of angina pectoris.*

DURING THE ATTACK. Electrocardiograms taken during attacks occurring naturally, or induced by smoking, show considerable displacement of the RS-T junction in either an upward or downward direction but no Q waves (103). Attacks of cardiac pain can often be reproduced by exercise, and in many *cases similar displacements* are found. The T wave may become diphasic or

weather. They are especially liable to occur if exertion is under- ... the process of digestion itself entails a ... the heart. Patients often ... though the onset is abrupt, the pain increases in intensity and very soon becomes intolerable if the exertion is not stopped

Type of Pain The pain is usually described as a "tightness" or "pressure"; as if there was something inside which was too big for the chest to hold. It may develop into an intense constriction. In many attacks, however, a dull ache only is felt, and occasionally a burning sensation is experienced. The pain is never stabbing in character; but is continuous until the exertion ceases. Sometimes dyspnœa accompanies the pain and the patient may be uncertain as to which makes him stop. Especially when emotion is a factor the patient may refrain from all movement, and even respiration may be restricted. This contrasts with the restlessness of many patients with infarction. In cases associated with emotion there may also be a sense of impending dissolution, and sweating and pallor may be conspicuous. These features are probably due to the secretion of adrenalin.

Duration. In angina of effort the pain does not usually last more than a few minutes, and passes off quickly as the exertion ceases If the attack lasts longer than fifteen minutes the possibility of infarction should be considered. On the other hand, a pain in the chest lasting less than a minute is seldom due to angina pectoris. Sometimes a patient is able to continue his exertion and walk off his pain. The fact that a raised RS-T junction sometimes fell to normal during the anoxæmia test suggests that some compensatory mechanism increasing the coronary flow may operate in these cases (107).

Other Findings. The blood cholesterol was raised in rather over half of the cases in one series (103). This may account for the fact that a large proportion of patients with hereditary xanthomatosis, which is due to hypercholesterolæmia, suffered from angina pectoris (114) An association with herpes zoster having a distribution similar to that of the pain has been noted (115).

ANGINA AT REST Apart from the attacks brought on by emotion, induced by smoking, or caused by conditions associated with extreme tachycardia, anginal attacks may ...

a depressor mechanism. Similar attacks have been recorded in congenital heart disease with an undeveloped right coronary artery (110). In mitral disease angina pectoris is almost unknown.

Anæmia. When the hæmoglobin value falls below 50 per cent cardiac pain on exertion may occur. Myocardial anoxæmia through the diminished power of the blood to carry oxygen is the cause. If coronary artery disease is present too, pain will be felt with a lesser degree of anæmia.

Hypoglycæmia. An overdose of insulin may cause an anginal attack. Very rarely attacks form part of the syndrome of spontaneous hypoglycæmia.

Tachycardia. A rapid rate such as occurs in prolonged attacks of paroxysmal tachycardia, may occasionally give rise to angina. The diminished output leads to insufficient filling of the coronary vessels. Angina pectoris does not occur with auricular fibrillation.

Spasm. Attacks with electrocardiographic changes have been recorded in subjects sensitive to tobacco, after smoking a cigarette (103, 111). Since these attacks occurred at rest, it would seem that they must be ascribed to spasm of the coronary arteries.

Diagnosis. The pain of angina pectoris has well defined characteristics and the diagnosis can usually be made from the history alone.

Angina of Effort. Information should be sought on the following points: the site of the pain: the mode of onset. the type of pain; its duration.

Site of Pain. The pain is substernal. Often it is described as being felt over the heart, but questioning will elicit the fact that it spreads across the mid-line. Occasionally it is felt chiefly at some other point, such as the jaw Cases have been recorded where it was confined to one or both arms (112). If severe, the pain radiates over the upper chest and down the ulnar side of the left arm, in the area supplied by the first two left dorsal roots. Tingling or numbness are also felt at the elbow or wrist. Sometimes there is a spread to the right side over the corresponding areas. In congenital dextrocardia, the pain has been noted on the right side.

Mode of Onset. The pain is brought on by exertion or emotion. As with dyspnœa, it is first noticed while walking up hills, later on the level. Attacks come on more easily in cold or windy

weather. They are especially liable to occur if exertion is undertaken soon after a meal, as the process of digestion itself entails a considerable increase in the output of the heart. Patients often attribute their pain to indigestion. Although the onset is abrupt, the pain increases in intensity and very soon becomes intolerable if the exertion is not stopped.

Type of Pain. The pain is usually described as a "tightness" or "pressure"; as if there was something inside which was too big for the chest to hold. It may develop into an intense constriction. In many attacks, however, a dull ache only is felt, and occasionally a burning sensation is experienced. The pain is never stabbing in character; but is continuous until the exertion ceases. Sometimes dyspnœa accompanies the pain and the patient may be uncertain as to which makes him stop. Especially when emotion is a factor the patient may refrain from all movement, and even respiration may be restricted. This contrasts with the restlessness of many patients with infarction In cases associated with emotion there may also be a sense of impending dissolution, and sweating and pallor may be conspicuous. These features are probably due to the secretion of adrenalin

Duration. In angina of effort the pain does not usually last more than a few minutes, and passes off quickly as the exertion ceases. If the attack lasts longer than fifteen minutes the possibility of infarction should be considered. On the other hand, a pain in the chest lasting less than a minute is seldom due to angina pectoris. Sometimes a patient is able to continue his exertion and walk off his pain The fact that a raised RS-T junction sometimes fell to normal during the anoxæmia test suggests that some compensatory mechanism increasing the coronary flow may operate in these cases (107).

Other Findings. The blood cholesterol was raised [illegible]

[illegible]

[illegible] ...æmia, suffered from angina pectoris (114) An association with herpes zoster having a distribution similar to that of the pain has been noted (115).

ANGINA AT REST. Apart from the attacks brought on by emotion, induced by smoking, or caused by conditions associated with [illegible]

sleep. They are found fairly frequently in association with syphilitic aortic reflux. In one series of a hundred cases of syphilitic angina pectoris, two-thirds had attacks at night (116). Patients who suffer from these attacks have reached the stage when such minor causes as a bad dream, or overloading of the stomach, or even slipping into an uncomfortable position during sleep, may be sufficient to precipitate an attack. The *prognosis is bad, and* death is imminent.

Nocturnal attacks may also be due to paroxysms of tachycardia or to spontaneous hypoglycæmia. In some cases the adoption of a recumbent position will cause pain almost at once (angina of decubitus). One patient had angina with electrocardiographic changes if he reclined with his feet raised (102).

Differential Diagnosis. PANNICULITIS. Submammary pain on the left side is a common complaint in women. It consists of a persistent dull ache which is often worse on exertion or emotion. This type of pain is often due to panniculitis. The apical region is tender to pressure, and palpation of the tender area reproduces *the pain about which complaint is made. Nearly every patient is* exact about this, which makes the differential diagnosis comparatively easy.

Fibrositis may involve the intercostal muscles round the sternochondral junctions in the second, third and fourth left spaces. This may lead to precordial pain on exertion or emotion, due to the fuller movements of the chest accompanying increased respiration. When the fibrositis affects the pectoralis minor, the pain is in the upper chest and is referred down the left arm. But again palpation of the tender spots will reproduce the pain, and the statement of the patient can be relied upon. If he has angina, he will say that his real pain is quite different. Both these conditions *are also found in the right side though less often*, but the patient does not associate the pain from them with his heart.

PLEURISY. Obscure pleurisy may occasion difficulties. The pain has a close relation to the phases of respiration.

GASTRIC AND ŒSOPHAGEAL PAIN. Stabbing pains in the region of the apex occur frequently. They probably arise in the stomach, and are of no significance.

Burning pain arising from the stomach, or reflexly from the gall-bladder, may suggest angina, if the pain occurs some time

after food, and the patient associates it with exertion. Disease of the gall-bladder and angina may co-exist, and the patient may suffer from both types of pain. The symptoms are then very hard to disentangle. Disease of the gall-bladder occurs twice as often in those with lesions of the coronary arteries as in those with normal arteries (117) There is no evidence that one causes the other, but it may be that some common factor, such as the vagus, operates in both. Both may have hypercholesterolæmia. The pain arising from herniation of the œsophagus or diaphragm may be difficult to distinguish clinically from angina, but radioscopy after barium will provide a clue to the diagnosis.

Treatment. GLYCERYL TRINITRATE is the most satisfactory drug to stop the attack. Tablets of 1/100 or 1/200 of a grain when chewed and dissolved in the mouth act in two or three minutes. The effect lasts about fifteen minutes, and intelligent patients can use the drug to prevent attacks by taking a tablet shortly before he moment at which experience has taught them to expect pain. 'he drug is not cumulative, and as many tablets as are needed an be taken each day. Octyl nitrite, inhaled, acts rather quicker than nitro-glycerine (118) It is supplied in tubes and s convenient to use. Amyl nitrite, the most potent vasodilator of all, is of especial value in attacks associated with a *rise in* blood pressure

AVOIDANCE OF ATTACKS. The patient should be instructed as to the nature of his attacks, and warned not to attempt exertion soon after meals. Meals should be taken dry, and the stomach must not be overloaded at any time. A reduction in weight, in those who are obese, will result in an increased effort tolerance. Especial care should be taken in cold weather: a hot drink can be taken before going out. An abdominal belt may help (119). Smoking should be allowed only after meals. Many patients find they are better without it altogether, and give it up. Alcohol in moderation does no harm; whiskey is often beneficial.

XANTHINE COMPOUNDS. The routine administration of xanthine compounds lessens the frequency of attacks. This has been controlled by electrocardiograms taken after exercise (120), and after anoxæmia (121), as well as by the increased tolerance of the patient. Some improvement was noted after theobromine sodium

gr. vi, each taken four times daily. Patients with less severe angina did best, but the response to the different compounds varied in different patients. In addition to these drugs, we have found quinidine, gr. vi, four times daily, to be of some use. In anxious patients phenobarbitone helps considerably.

THIOURACIL. Thyroidectomy used to be performed in cases of intractable angina pectoris, the aim being to reduce the metabolic needs of the body, and with them the speed of the circulation, to a level within the compass of the damaged heart. The same result can now be obtained with thiouracil. Thirty-seven cases were given thiouracil in initial doses of 0.6 or 0.4 g. daily with 0.1 to 0.2 g. as maintenance doses (122). Treatment was continued for about six months and improvement was noted in 25, or about two-thirds of the cases, after an average period of four weeks. The failures included five patients in whom the drug had to be stopped in a few days on account of fever, and three who developed neutropenia later. The B.M.R. fell and the blood cholesterol rose in all cases, and the patients gained weight, but subjective improvement bore little relation to the grade of myxœdema induced. Thiouracil is certainly useful for patients with angina in whom other forms of treatment have failed, but close supervision is necessary as the white cell count may fall at any time. There is also a tendency for œdema to develop, especially in the lungs. The underlying disease is not checked in its progress, so treatment may have to go on indefinitely.

Nicotinic Acid Infusions have been suggested (123). 150 mg. are dissolved in 300 ccs. of saline and given intravenously by drip infusion. The dose is increased gradually to 300 mg. in a course of six infusions given at weekly intervals. The results are uncertain but some patients respond well, losing their pain. Nicotinic acid by mouth is useless.

SURGICAL MEASURES. Various surgical measures have been devised to stimulate the growth of new vessels (124). The surface of the heart has been abraded by introducing powdered beef bone, or grafts have been taken from the pericardium, or muscle of the chest wall, or from the omentum. Since only intractable cases, who have failed to respond to all forms of medical treatment, have been submitted to operation, the mortality is high, reaching 50 per cent. Although some have improved, the surgical treatment of

angina pectoris must be regarded as being still in the experimental stage, and no recent developments have been reported.

Prognosis. The prognosis is very variable. There is always a risk of infarction, and sudden death from syncope, or ventricular fibrillation, may occur in any severe attack. The course is slowly progressive as a rule. Attacks of angina pectoris may clear up if the patient subsequently has an occlusion, and attacks which arise following an occlusion may cease after a time. The average expectation of life is over eight years, and some cases live much longer (125) As a general rule the frequency of the attacks and the amount of effort required to produce them are good guides to prognosis. Nocturnal attacks occurring regularly have the worst prognosis

REFERENCES

1 [illegible] J., 19, 1.
[illegible] Ass., 116, 91.
5 HAMMAN (1941) *Amer. Heart J* 21 401
6 [illegible] 84
[illegible] 675
[illegible] 49
[illegible] *eart J.*, 18, 647.
15 [illegible] 0.
16
17
18
19
20 [illegible] *Amer med Ass* 117, 2019.
21 STEAD, EBERT (1942) *Arch intern Med*, 69, 369.
22 COOKSON (1942) *Brit Heart J*, 4, 163
23 WEISS (1939) *Amer Heart J* 17 103
24 STEWART [illegible]
25 [illegible] 32
26 [illegible] *med Ass*, 118, 779
[illegible], KOSSMANN, HECHT,
27 [illegible] *Amer. Heart J*, 27, 19
[illegible] 7, 164.
[illegible] *Heart J.*, 27, 803
[illegible] *Brit Heart J*, 1, 45
[illegible] *mer. Heart J*, 15, 235
[illegible] J., 32, 163
[illegible] In Press
35 GOLDBERGER (1942) *Amer Heart J*, 23, 483
36 WOLFERTH, WOOD (1941) *Amer Heart J*, 22 451

37 Goldberger (1942) *Amer Heart J.*, **24**, 378
38 Butterworth, Poindexter (1946). *Amer Heart J.*, **32**, 681
39 Nyboer (1941) *Amer Heart J*, **22**, 469
40. Ungerleider, Gubner (1947) *Amer Heart J*, **33**, 807
41. Myers, Oren (1945) *Amer Heart J*, **29**, 708
42 Wood, Wolferth, Bellet (1938) *Amer Heart J*, **16**, 387
43. Thomson, Feil (1944) *Amer J med Sci*, **207**, 588
44 Rosenbaum, Wilson, Johnston (1946) *Amer Heart J.*, **32**, 135
45 Master, Dack, Jaffe (1938) *Amer Heart J*, **16**, 283
45a. Roesler, Dressler (1947) *Amer Heart J*, **34**, 817
46 Young, Koenig (1944) *Amer Heart J*, **28**, 287
47. Cushing, Feil, Stanton, Wartman (1942) *Brit Heart J.*, **IV**, 35
48 Bellet, McMillan (1938) *Arch intern Med*, **61**, 381
49 Langendorf (1941) *Amer Heart J*, **22**, 86
50. Barnes, Burchell (1942) *Amer Heart J*, **23**, 247
51 Vander Veer, Norris (1939) *J Amer med Ass*, **113**, 1483
52. Robb, Robb (1939) *Amer J med Sci*, **197**, 7
53 Robb, Robb (1939) *Amer J med Sci*, **197**, 17
54 Feil, Cushing, Hardesty (1938) *Amer J Heart*, **15** 721
55 Strauss (1940) *Amer J med Sci*, **200**, 474
56. Weinberg, Katz (1941) *Amer Heart J*, **21**, 699.
57. Vander Veer, Edwards (1939) *Amer J med Sci*, **197**, 663
58. Robinson, Contratto, Levine (1939) *Arch intern Med*, **63**, 711.
59 Master (1941) *Amer J Roentgen*, **45**, 350
60 Master, Gubner, Dack, Jaffe (1940), *Amer Heart J*, **20**, 475.
61. [illegible] *Amer Heart J.*, **19**, 464
62 [illegible] *mer Heart J*, **19**, 453
63 [illegible] *Heart J*, **18**, 8
64. [illegible] *Amer Heart J*, **16**, 133
65 [illegible] , 579
66 Thomson (1947) *Lancet*, **1**, 630
67 Miller (1945) *Amer J med Sci*, **209**, 211
68 Smith (1939) *Amer Heart J*, **17** 735
69 Bayley, Fader (1941) *Amer Heart J*, **21**, 238
70 Wood, Livezey (1942) *Amer Heart J*, **24**, 807
71 Moolten (1942) *Arch intern Med*, **69**, 108
72 Wood (1944) *Brit Heart J*, **4**, 191
73 Askey, Neurath (1945) *Amer Heart J*, **29**, 575
74 Edeiken (1943) *Amer J med Sci* **205**, 52
75 [illegible] *tern Med*, **68**, 913
76. [illegible] *J*, **24**, 4
77. [illegible] *J med Sci*, **196**, 513
78 [illegible] *Heart J*, **33**, 443
79 [illegible] **23**, 362
80 [illegible]
81. [illegible] *tern Med*, **14**, 100
82 [illegible] 38) *Quart J Med*, **7**, 455
83 [illegible]
84 [illegible] , **71**, 502
85 [illegible] *rn Med*, **66**, 800
86 [illegible] **14**, 540
87 [illegible]
88 [illegible] *Heart J*, **23**, 715
89 [illegible] *Heart J*, **23**, 637
90 [illegible] *Heart J*, **12** 549
91 [illegible] seases"
92. [illegible] *J*, **1**, 621
93 [illegible] 45) *Surgery*, **17**, 207.

[illegible] (1946) J. Amer. med. Ass. 130, 308

106 LEVY, BRUENN, RUSSELL (1939) *Amer. J. med. Sci.*, 197, 241
107 PATTERSON, CLARK, LEVY (1942). *Amer. Heart J.*, 23, 837.
108 LEVY, WILLIAMS, BRUENN, CARR (1941) *Amer. Heart J.*, 21, 634
109 LEWIS (1929-31) *Heart*, 15, 305
110 WHITING (1937) *Amer. Heart J.* 14, 104
111 BRYANT, WOOD (1947) *Amer. Heart J.*, 34, 20
112 SPILLANE, WHITE (1940) *Brit. Heart J.*, 2, 123
113 RISEMAN, BROWN (1937) *Amer. Heart J.*, 14, 331.
114 MULLER (1939) *Arch. intern. Med.*, 64, 675
115. SPILLANE, WHITE (1939) *Brit. Heart J.*, 1, 291
116 JONES, BEDFORD (1943) *Brit. Heart J.*, 5, 107
117 WALSH, BLAND, TAQUINI, WHITE (1941) *Amer. Heart J.*, 21, 699
118 [illegible] *Heart J.*, 22, 519
119 [illegible]
120 [illegible] *Heart J.*, 22, 494
121 [illegible] *mer. Heart J.*, 22, 232
122 [illegible]
123 [illegible]
124 BECK (1941) *Amer. Heart J.* 22, 539
125 WHITE (1944) "Heart Disease" *3rd Edit.*, p. 830

CHAPTER VIII

BRADYCARDIA AND DISORDERS OF CONDUCTION

Bradycardia and Disorders of Conduction
Postural Hypotension

UNDER this heading are considered sinu-auricular block and nodal rhythm, auriculo-ventricular heart block, and bundle branch block. The presence of disorders of conduction may show that the myocardium is diseased, but this does not necessarily mean that the heart cannot work quite efficiently. Bradycardia from other causes is usually harmless.

Transmission of the Impulse. The impulse for contraction arises at the sinu-auricular node of Keith and Flack (1910), which lies at the junction of the superior vena cava and right auricle. It spreads thence throughout the walls of the auricle, where there is no special path to conduct it. At the base of the auricular septum just in front of the opening of the coronary sinus, the muscle fibres of the auricle run together and interlace to form a definite strand of tissue. This structure is known as the auriculo-ventricular node of Tawara (1906). From it the impulse is transmitted to the ventricles by the auriculo-ventricular bundle of Kent and His (1893), which runs forward and slightly downwards under the median cusp of the tricuspid valve on to the ventricular septum. The central fibrous body of the heart lies on its left, and the root of the mitral valve is not far off. The bundle passes behind, and immediately below, the pars membranacea septi. At this point it divides into two branches. The right branch runs for some distance as a single strand down the septum, under the endocardial lining of the right ventricle. There it breaks up, a considerable strand running across the moderator band. The left branch passes under the pars membranacea septi to the left ventricle, where it lies just under the commissure of the right anterior and posterior cusps of the aortic valve. At this point it breaks up into a widely-spreading fan of fibres, which curve down

the septum under the endocardium of the left ventricle. The twigs of both branches anastomose with the network of Purkinje lining the ventricles.

The node receives its blood supply from the circumflex branch of the right coronary. Septal twigs from the anterior descending branch of the left coronary penetrate also to supply the lower part of the bundle. Many nerve fibrils and ganglion cells are found in the region of the node. The fibres are derived from the vagus and sympathetic.

This traditional view of the conducting tracts in the ventricles has recently been challenged (1, 2). Glomset was unable to find any satisfactory evidence of a special conducting system in the ventricles in the hearts of dogs or in man. He points to the disturbing fact that while Keith and Lewis originally described the bundle as a strand which could be seen by the naked eye beneath the endocardium, serial sections have been required by all writers since 1920 to insure that the track of the bundle is not lost. He agrees that many nerve fibrils and ganglion cells are found in the auriculo-ventricular groove, and considers that conduction thence takes place along the muscle bundles described by Robb. This work has not yet been confirmed from other sources

Bradycardia Due to Vagal Influence. An important action of the vagus in man is to depress the rate of impulse formation at the sinu-auricular node. Variation in the vagal tone causes irregularities in the cardiac rhythm.

RESPIRATORY [illegible]

[illegible]

[illegible] may be reduced very considerably. In itself this is of no significance. It may be conspicuous after infections, especially if the rate of the heart is slow. Occasionally the irregularity is so striking that some serious disorder such as fibrillation may be suspected: this may occur if the breathing is irregular. Some children do not show sinus arrhythmia to any degree. After puberty, sinus arrhythmia is less common, although it may be present at any age.

PHASIC SINUS ARRHYTHMIA. The second type of sinus arrythmia has no relation to the phase of respiration. It is known as "phasic



FIG 34.
Sinu-auricular block

sinus arrhythmia." *In this form the vagal tone increases for some* seconds and then fades again. It may occur as the result of the *stimulating effect of digitalis on the vagus* *There, too, the condition* has no importance except as an indication of the effect of digitalis. It occurs in convalescence after fevers and as a result *of influenza : it is the cause of the bradycardia of jaundice.*

SINUS BRADYCARDIA. In the adult the rate of the heart is *usually somewhere about 70.* *But some people have a much slower pulse. In them the slow rate is due to a high vagal tone.* The condition is common in athletes. Large men often have slow pulses. The term commonly used to describe this condition is *"sinus bradycardia."* *Again it is of no importance.* *The rate is* usually about 40 to 50. The rhythm is rarely completely regular. There is the usual quickening on exertion or emotion.

Sinu-Auricular Block is present when a complete cardiac cycle is missed. It gives rise to an irregularity impossible to distinguish clinically from A-V heart block with dropped beats. The electro*cardiogram shows that the auricular (P) wave is absent as well* as the ventricular deflections, the impulse having failed to start (Fig. 34). After a pause the next cycle appears in its proper place. *The cycles before the missing ones sometimes come rather more* quickly than usual. Those following the gap are a little slower. This variation in spacing of the cycles is very like that seen in the *case of ventricular beats in partial heart block when beats are* dropped. *On this resemblance it was suggested by* Wenckebach that there might be a block between the sinus and the auricle. *Sometimes many cycles are missed.* *If every alternate beat is* missing, a bradycardia of about thirty-five results. This is sometimes found in athletes during training. Exercise will cause an abrupt doubling of the rate.

Sinu-auricular block does not signify heart disease. It is sometimes found in patients who are suspected of having Stokes-

Adams disease from the slow and irregular pulse. The condition is probably wholly vagal in origin, and can readily be abolished by atropine.

Auricular Standstill, in which the auricular contractions fail altogether, is very rare, and is due to poisoning with digitalis or quinidine (3). Unless the ventricles commence at once to beat independently, death will result, and this may account for some of the unexplained sudden deaths during the administration of digitalis (4)

NODAL RHYTHM. If the sinu-auricular node is depressed by vagal action, a lower centre may take on the role of pacemaker.



FIG 35

Nodal Escape The third, fourth and eighth complexes arise from the A-V node *The fifth complex* (*) is a response to P_1



FIG 36

Nodal Rhythm Note inverted P waves (P_1) following the ventricular deflections

This is often the A-V node, and the heart then beats to a "nodal rhythm" The rate is usually about *50*.

Electrocardiograms *show* normal ventricular complexes with inverted P waves, signifying *retrograde* spread through the auricle, occurring either just before, or just after, the QRS. Alternatively, *they may* be buried in the QRS and not appear at all.

In young people nodal *rhythm* may sometimes be maintained for long periods More often it appears for a single beat



FIG. 34
Sinu-auricular block

sinus arrhythmia." In this form the vagal tone increases for some seconds and then fades again. It may occur as the result of the *stimulating effect of digitalis on the vagus. There, too, the condition* has no importance except as an indication of the effect of digitalis. It occurs in convalescence after fevers and as a result of influenza : it is the cause of the bradycardia of jaundice.

SINUS BRADYCARDIA. In the adult the rate of the heart is usually somewhere about 70. But some people have a much slower pulse. In them the slow rate is due to a high vagal tone. The condition is common in athletes. Large men often have slow pulses. The term commonly used to describe this condition is "sinus bradycardia." Again it is of no importance The rate is usually about 40 to 50. The rhythm is rarely completely regular. There is the usual quickening on exertion or emotion

Sinu-Auricular Block is present when a complete cardiac cycle is missed. It gives rise to an irregularity impossible to distinguish clinically from A-V heart block with dropped beats. The electrocardiogram shows that the auricular (P) wave is absent as well as the ventricular deflections, the impulse having failed to start (Fig. 34). After a pause the next cycle appears in its proper place. The cycles before the missing ones sometimes come rather more quickly than usual. Those following the gap are a little slower. This variation in spacing of the cycles is very like that seen in the case of ventricular beats in partial heart block when beats are dropped. On this resemblance it was suggested by Wenckebach that there might be a block between the sinus and the auricle. Sometimes many cycles are missed. If every alternate beat is missing, a bradycardia of about thirty-five results. This is sometimes found in athletes during training. Exercise will cause an abrupt doubling of the rate.

Sinu-auricular block does not signify heart disease. It is sometimes found in patients who are suspected of having Stokes-

in one case (7). Rarely the sinus may be irritated by pressure from a tumour on the neck. The result of cardiac arrest is a syncopal attack.

Cardiac Syncope may be caused by several circulatory disturbances which lead to cerebral anæmia. The most dangerous is the Stokes-Adams syndrome, since if the idioventricular centre does not start within two minutes, death will result. Extreme tachycardia, such as occurs in an attack of ventricular fibrillation or 1-1 flutter, causes syncope as the blood flow to the brain practically ceases. Old people with calcareous aortic stenosis are liable to have syncopal attacks (p. 62), or an attack may mark the onset of a coronary occlusion (p. 195).

An ordinary faint is due to a diminished volume of blood returning to the heart. It is seen in its simplest form in those who faint after standing for some time without movement. In these the cardiac output and stroke output was found to fail by 30 per cent (8). Before they collapsed, pallor and sweating were present indicating a stimulation of the sympathetic. This seemed to be an attempt to compensate by vasoconstruction for the lack of muscular contractions which assist the return of the blood against gravity through the veins. Sometimes there is *tachycardia* which aggravates the situation by shortening the diastolic *filling time*; but usually bradycardia results from vagal influence. The blood *pressure* is low.

Emotional causes, such as agitation, pain, disgust or surprise, are often exciting factors. Presumably they lead to a pooling of the blood in the splanchnic area. The attack may be very sudden, and then the vagal effect predominates. Patients are more liable to faint in hot weather or in *stuffy* atmospheres owing to the dilatation of the skin vessels which occurs under these conditions; an empty stomach also increases the liability. A [illegible] d of [illegible] some [illegible] some [illegible], but [illegible] uncommon in the aged and may be prolonged.

Immediate relief may be gained by laying the patient flat. Sometimes a certain degree of faintness may persist for several hours. An injection of adrenalin and atropine is the best treat-

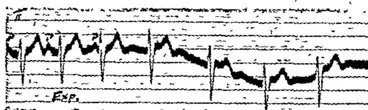


Fig 37

Nodal Escape As the vagus slows the heart on expiration, the auriculo-ventricular node escapes The P waves are then buried

the sinus impulse is unduly delayed as in forced expiration (nodal escape) (Fig 37). In sinus arrhythmia alteration in the shape of the P wave is often seen during the expiratory pauses, suggesting a shift of the pacemaker to another level in the S-A node or to another part of the auricle.

Coronary Sinus Rhythm originates in the upper part of the A-V node extending up the sinus of the coronary vein (5) The waves are positive in lead I but sharply inverted in leads II and III. (Fig. 38). The P-R interval is normal, and so is the rate

Nodal rhythm, and migrations of the pacemaker in the auricle, are of no clinical significance. They can usually be abolished by exercise, and nearly always by atropine.

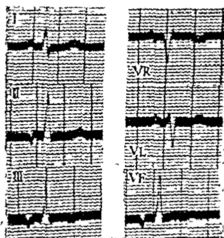


Fig 38

Coronary sinus rhythm Note inverted P waves in leads II, III and VF The heart is vertical Three minutes after injection of atropine, P waves became positive

A nodal rhythm at an unusually fast rate is associated with interference dissociation (p 241); nodal rhythm may also lead to *reciprocal rhythm* (p. 240). In both these rare instances *retrograde heart block* between the A-V and sinus nodes *is present in addition.*

Cardiac Arrest If the *vagal influence is sufficiently strong,* asystole of the whole *heart may occur* (6) In sensitive individuals asystole may *follow carotid sinus pressure* (p. 298). Standing erect after hard physical work brought on asystole lasting 19 seconds

The toxin of any acute infection may interfere with the cells transmitting the impulse Heart block may be found in severe anæmia. Complete heart block has been recorded in hyperthyroidism, disappearing under iodine therapy (12), and as the result of thiouracil therapy (13). Syphilis is occasionally a cause of heart block in middle age. A subacute septic endocarditis may spread down to the top of the septum, or an infection may burrow in from the mitral valve.

Congenital Defects Heart block may be associated with a defect in the interventricular septum. The septum is incompletely developed at the top, leaving a hole where the pars membranacea septi should be (p. 11) Complete dissociation of the auricular and ventricular rhythm is the result. Congenital complete heart block has been diagnosed before birth by a sudden halving of the fœtal heart rate (14).

Drugs. Drugs of the digitalis group depress conductivity indirectly through the vagus, and directly by their action on the junctional tissues

Latent Heart Block or Prolongation of the P-R Interval. It is not possible to subdivide the time taken by the impulse to pass through the auricular muscle, and thence down the bundle to the ventricles. Measurements in the electrocardiograms are taken from the beginning of the auricular systole (P) to the beginning of the ventricular systole (Q or R). This period is known as the P-R or P-Q interval

In a small proportion of cases measurements of the P-R interval may be incorrect if taken from lead II, since a Q wave in lead I may cancel the corresponding R in lead III (15) This will cause an abbreviation of the QRS in lead II, the initial phase being isoelectric, with a false lengthening of the P-R in this lead. To obtain the correct value, the duration of the longest QRS in any lead should be subtracted from that of the longest P-S Lead III usually provides the most accurate P-R intervals in lead I they are often too short

The average normal P-R interval is about 0 16 second. It varies both with the size of the individual and with the rate of the heart. In young infants it is usually below 0.12 second. in children it seldom exceeds 0 19 second, but may do so if the vagal action is strong. Thus 8 out of 150 apparently normal children had P-R

ment. Hypoglycæmia must be remembered as an occasional cause of syncope, the result, in some cases, of hyperinsulinæmia.

Auriculo-Ventricular Heart Block

When there is impairment of conduction of the impulse from the auricles to the ventricles, A-V heart block is said to be present. The impulse may only be delayed in its passage—this is prolongation of the P-R interval, or latent heart block; or some impulses may fail to get through—then there is incomplete or partial heart block. Finally, all the impulses may be blocked, and the ventricles respond to an idioventricular centre, the auricular and ventricular rhythms being dissociated—this constitutes complete heart block.

Aetiology. Vagal Effect. Stimulation of the vagus depresses conductivity from auricle to ventricle. A few rare instances have been known in which a tumour of the neck produced complete dissociation of auricles and ventricles. Stimulation of the carotid sinus, or ocular compression, may cause reflex depression of conduction by increasing the vagal tone.

Vascular Lesions. In elderly people, obliterative processes in the arterioles, accompanied by replacement fibrosis, may cut off the blood supply to the bundle, and thus depress its function or cause it to degenerate. This is much the commonest cause of heart block, accounting for 65 per cent of cases of complete block (9). A septal infarct may cause complete dissociation or bundle branch block.

Toxic and Inflammatory Causes. The myocarditis of acute rheumatism is especially liable to cause A-V heart block. Latent heart block is common, and probably more cases would show prolongation of the P-R if electrocardiograms were taken more frequently during the acute phase. Dropped beats are not uncommon and complete heart block may occur. This action is, in part, due to the vagus since the A-V block can nearly always be abolished temporarily by the intravenous injection of atropine, gr. 1/30th (10).

The toxin of the Klebs-Loeffler bacillus of diphtheria is well known to cause heart block. Complete heart block is perhaps the most dangerous complication of diphtheritic myocarditis (p 101). If recovery takes place, the heart block usually clears up completely, but occasionally the defects of conduction persist (11).

premature beats where the ventricular response is blocked. Sinu-auricular block is indistinguishable clinically from A-V heart block.

Dropped beats are usually transient. They are associated with infections such as acute rheumatism or tonsilitis. Other cases occur during digitalis overdosage, but here again, an infection is often present as well (19). In both these groups the heart block often clears up. In older people dropped beats are less frequent, and in them the latent heart block persists, or else the block may increase to a 2-1 block or to complete block. 2-1 block, in which every alternate impulse fails to get through, is relatively stable and may persist for long periods, even for years. Auricular systole may be heard between the ventricular beats. High grades of block, such as 3-1 or 4-1, are rare, the patient usually passing straight on to complete heart block.

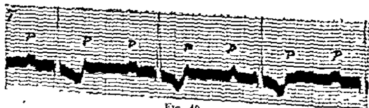


FIG 40

Dropped beats Alternate impulses are blocked, causing 2-1 heart block. P-R is prolonged to 0 32 sec Ventricular rate between 50 and 60 Depression of T waves indicates the effect of digitalis, which has caused the block

Dropped beats occur under two conditions. They may follow a cycle of progressive lengthening of the P-R interval (Wenckebach period) In this way every third beat may be dropped (3-2 heart block), or every fourth (4-3 heart block) The increasing intervals are fairly constant and can be roughly predicted according to a mathematical formula (20). After the dropped beat the conduction improves. But in about 12 per cent the beat is dropped abruptly without any previous lengthening of the P-R (14). In this group it seems probable that the impulse fails owing to a depression in excitability in the ventricular muscle rather than to a sudden change in conductivity. Complete block more commonly follows this type. Cases with progressive lengthening of the P-R are best explained in terms of increasing refractoriness of the myocardial

intervals in excess of 0.19 second, and in one it was 0.24 second: 8 out of 140 rheumatic children, without activity, had increased P-R intervals, the maximum being 0.40 second. Mild exercise in one child increased the P-R by 0.17 second (16). Cases have been recorded of healthy young men who had P-R intervals of 0.40 second when supine but normal intervals when upright; one in addition had dropped beats (17). In large men with slow hearts the P-R interval may exceed 0.20 second. Generally, however, a P-R interval over 0.20 second is considered to be prolonged: although a small increase should not be taken by itself to signify heart disease.

Prolongation of the P-R over 0 20 second has been termed latent heart block, since graphic records are needed for the diagnosis (18). An exception to this occurs infrequently in mitral stenosis, when the presence of heart block may be surmised if an

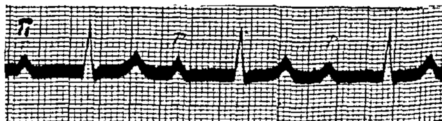


FIG 39

Lead II, showing prolongation of P-R interval to 0 41 sec

appreciable interval elapses between the presystolic murmur and the mitral first sound. On rare occasions the sound of auricular systole may be heard before the first sound, causing a third sound to be heard. In latent heart block the P-R interval may reach 0.40 second, and we have seen it as long as 0.60 second, but it is usually from 0.20 to 0.26 second. It often remains constant for years but may gradually increase (Fig. 39).

Incomplete Heart Block with Dropped Beats. Dropped beats can usually be recognised clinically since a ventricular systole is missing. No pulse wave will reach the wrist, and on auscultating over the heart no ventricular contraction will be heard. It is important to confirm the gap in the pulse rhythm by auscultation, for premature beats may fail to reach the wrist, but they will usually be audible over the heart. Exceptions to this are auricular

The clinical recognition of complete heart block is not difficult. In addition to the slow rate the first heart sound varies in intensity, being louder when it coincides with an auricular systole. In the long diastole muffled sounds of other auricular systoles are often audible. Venous waves, when visible in the jugular veins, can be seen to have no relation to the ventricular systole and they vary in size, apart from respiration, as the tricuspid valve is open or closed. These signs of auricular activity, which were first noted by Stokes, are, of course, absent if the auricles are fibrillating, and they are not easy to appreciate if the ventricular rate is over 50.

Electrocardiograms show that the auricular and ventricular rhythms have no relation to each other, and that the auricular rhythm is the faster. The auricular rhythm is often slightly irregular, since the P-P intervals with ventricular contractions between them are shorter than those without (21). On screen examination both the auricular and ventricular rhythms can usually be seen clearly, the oscillating point being found in the region of the left auricular appendage just above the left ventricular border.

Complete heart block is usually permanent, the majority of cases being due to degeneration of the conducting tissues secondary to vascular lesions. After diphtheria and frequently after infarction, conduction returns to normal, if the patient survives the acute stage. In rheumatism, recovery is often incomplete, some latent heart block persisting. Bundle branch block is present in addition

...branches, the main stem being intact (22).

Intermittent Complete Heart Block. Complete heart block may alternate with normal rhythm. Syncopal attacks are likely to occur during the transition periods. Later complete heart block usually becomes established and the attacks then disappear (23). There is probably a progressive organic lesion in these cases as atropine has no effect on the attacks (24).

SUPER-NORMAL RECOVERY PHASE was a term used by Lewis to explain the fact that immediately after recovery from the refractory period, heart muscle may respond to stimuli which are below the normal threshold strength. In some rare cases paroxysms of

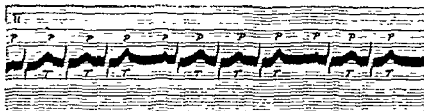


Fig. 41

Dropped beats The auricular rhythm is regular (P) but heart block causes prolongation of the P-R interval until the third or fourth is blocked P tends to be merged in the preceding T wave, and alters its shape

cells which finally reaches a point at which the impulse is not accepted. Following the rest so gained the cycle is repeated (Fig. 41).

Complete Heart Block. In complete heart block, the auricular and ventricular rhythms are dissociated (Fig. 42). The ventricles now beat to an idio-ventricular rhythm. The site of the new pacemaker is in the junctional tissues just below the block. The rate is usually from 30 to 40 beats a minute, but it may be 60 or more in congenital heart block, diphtheria, acute rheumatism and following cardiac infarction. The rhythm is regular, unless premature ventricular beats are present. The rate is unaffected by exercise, emotion, amylnitrite or fever. When the pacemaker is situated in the upper levels of the bundle, it is probably to some extent under the influence of the vagus, since atropine, gr. 1/30th intravenously, may cause some increase in the rate. The increase is greater if the initial rate is high. Adrenalin has but little effect on the rate unless it is low. The heart, in complete heart block, responds to exercise by increasing the stroke volume as the rate cannot be raised. The pulse pressure is usually high, owing to elevation of the systolic pressure.

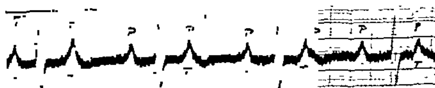


Fig 42

Complete heart block. Note slow alteration in time relationship of P and ventricular complex T waves are distorted by superimposed P waves

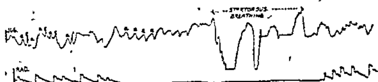


Fig 43

Tracing of jugular and radial impulses during a Stokes-Adams' attack, lasting 16 seconds Auricular contractions (*a*) can be seen in the jugular tracing until obscured by stertorous breathing, which ensues in eight seconds

Clinical Features. At the onset of the attack the patient suddenly turns pale and loses consciousness. If standing, he will fall to the ground. No pulse can be felt at the wrist: no sounds can be heard at the heart After a few seconds he may become cyanosed and considerable suffusion may be seen over the face and lips: or he may remain pale during the course of the attack. The eyes stare, or are rolled up The breathing next becomes stertorous, and after about 15 seconds clonic convulsions, mainly of the upper part of the body, ensue which last until the pulse returns, when consciousness is rapidly regained. During this time there may be incontinence of urine and fæces. There are no ill effects on the brain after an attack; the patient is himself again in a few moments (Fig. 43).

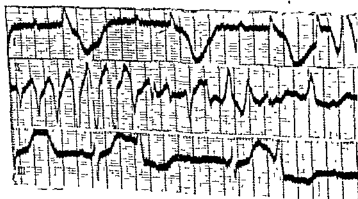


Fig 44

complete heart block occurred when the auricular rate slowed, and normal conduction was not established until an idio-ventricular beat came between 0.5 and 0.9 second before a P wave. Once established, normal conduction continued until the interval between the auricular beats exceeded 1.0 second, when conduction failed until another idio-ventricular beat with the same timing occurred (25). Similarly in complete heart block a Stokes-Adams attack may take place unless conduction is started by a suitably timed premature ventricular systole. Such premature systoles may, on occasion, be stimulated by the use of adrenalin (Fig. 47).

The Stokes-Adams Syndrome. The Stokes-Adams syndrome is *distinguished from other types of cardiac syncope by the fact* that the auricles continue to beat, although after 20 seconds of ventricular standstill the auricles are affected by asphyxia. They may beat more slowly or irregularly, or they may pass into flutter or fibrillation, or they may stop.

Stokes-Adams attacks always constitute a medical emergency. Unless a centre in the ventricle begins to beat at once when conduction fails, the patient will die. Recovery rarely takes place from ventricular standstill if it lasts more than a minute.

Attacks may be expected during the rapid development of severe degrees of heart block. Thus they complicate the heart block of diphtheritic myocarditis and of cardiac infarction, in which an element of shock enhances the cerebral anæmia by lowering the blood pressure (26), and are common in cases of intermittent complete heart block. In this type the attacks usually cease when complete heart block becomes established.

They may also arise during the course of complete or partial heart block when changing ventricular complexes of bundle branch type denote *multiple centres of impulse formation in the ventricles* (27). In these patients, attacks tend to recur and death nearly always takes place in an attack. A curious case *has been described* in which many syncopal attacks due to ventricular standstill occurred in a patient with a persistent sinus bradycardia, no heart block being present (28). The condition was attributed to a state of diminished excitability of all the pacemakers.

Lastly attacks may be caused by paroxysms of ventricular tachycardia or fibrillation complicating complete heart block.

of a progressive increase in the ventriculo-auricular conduction time, until finally an auricular impulse with an inverted P is followed by a second ventricular beat (R), the single impulse from the node having given rise to two ventricular contractions. The rhythm may occur every other beat, analogous to 2-1 forward block, or every 4th or 5th (Fig. 45). It is often associated with digitalis overdosage (30), and it is transient. In a patient with a patent ventricular septum, where it was found during digitalization, atropine was without effect (31).

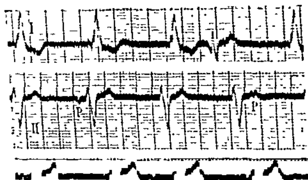


FIG 45
Reciprocal rhythm with a reversed Wenkebach period of five [illegible]

INTERFERENCE DISSOCIATION. In febrile infections, and especially in acute rheumatism (32), a nodal rhythm may occur at an unusually fast rate. The sinu-auricular node, which is depressed and so unable to maintain a rhythm fast enough for the needs of the body, activates the auricle at a slower rate. There is, therefore, dissociation between the auricular and ventricular rhythms, as in complete heart block, but with the difference that the ventricular rate is the faster. Retrograde heart block is here complete: the

ELECTROCARDIOGRAMS. Of the four types ventricular standstill is the most common (6). The P waves continue unaltered, or somewhat faster, in short attacks. In long attacks they may become slow and irregular, or fibrillation may supervene, or they may disappear. This is the type to be expected when conduction fails down the bundle and the idio-ventricular centre does not start at once.

Attacks may occur when the idio-ventricular rhythm is unusually slow. Faintness is felt when the ventricular rate is less than 20 a minute, and unconsciousness supervenes when it falls below 10.

In attacks that occur after the establishment of complete heart block, when bilateral bundle lesions may be present, there is often a shift in the impulse forming centre in the ventricle before the ventricular standstill. The pulse becomes irregular from ventricular premature beats, and then the new centre takes over at a faster rate. The rate may be in the neighbourhood of 60, or ventricular tachycardia or fibrillation with rates up to 300 may be present. When the tachycardia ceases, standstill follows. In this type unconsciousness may be prolonged up to seven minutes. The state of the cerebral arteries is important in determining the duration of unconsciousness (6). Lastly, the whole attack may be caused by ventricular tachycardia or fibrillation, or both, without standstill. This form may complicate heart block or occur when conduction is normal (29) (p. 292) (Fig. 44).

Retrograde Heart Block. In A-V nodal rhythm the stimulus, as well as passing down to the ventricles, spreads backwards to the auricles, with the result that they contract, and inverted P waves may either follow or immediately precede the QRS. But sometimes there may be progressive delay in the conduction to the auricles so that a reversed Wenckebach period results, which resembles partial retrograde heart block. In other cases the impulses from the node may not reach the auricles at all, which beat to their own sinus rhythm.

RECIPROCAL RHYTHM was used by Drury (1924) to describe a condition in which retrograde heart block reaches such a degree that the impulse from the node, having activated the auricle is able to spread down again and re-enter the ventricle which by that time is no longer refractory. The sequence of events is that

intensity of the first sound have also been noted. The dissociation lasts a few days only and requires no treatment as the patient will be confined to bed on account of the infection. As he recovers, the patient may pass through stages of reciprocal rhythm, nodal rhythm (Fig. 46B) and latent heart block with prolonged P-R interval, illustrating the nature of the disorder (33).

The opposite condition of retrograde conduction when orthograde conduction is blocked is seen sometimes in complete A-V heart block when inverted P waves deform the S-T interval about 0.16 second after R waves which follow the preceding P by about 0.50 seconds (34). This shows that the auricle has been activated from the ventricle, and may indicate a supernormal recovery phase in the auricle. Mechanical stimulation of the auricle by the ventricular contraction has been advanced as an explanation, but this is unlikely as the inverted P indicates a retrograde spread of the impulse (35)

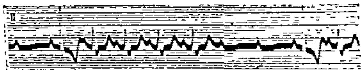


FIG 47

Stokes-Adams Disease Effect of adrenalin Note short runs of normal beats which begin with a premature ventricular systole, and continue until the auricular rate slows

Treatment of Heart Block. *Latent Heart Block* requires no special treatment. Syphilis should be excluded · digitalis may have to be stopped But digitalis in therapeutic doses does not augment heart block due to structural disease. In 16 cases in whom it was pushed to a point of nausea, the P-R interval was increased slightly in six only, while it was actually reduced in two, following clinical improvement (36).

Partial Heart Block with Dropped Beats is found mainly in infections and the patient should be confined to bed. Atropine, gr 1 30th–1/75th given intravenously will usually succeed in abolishing the heart block temporarily. Caffein sodium benzoate, given by intravenous injection in doses of 15 grs., abolished both the block and Cheyne-Stokes respiration in one case where 2-1 block or complete dissociation occurred during the apnœic phase

auricular waves (P) are slower and upright and unaffected by the faster ventricular rhythm. Forward conduction is not, however, obstructed, although the impulse may be delayed, and if an impulse from the auricle happens to arrive when the ventricle is not refractory an early ventricular beat results. The most likely moment is at the end of ventricular systole when the P wave and

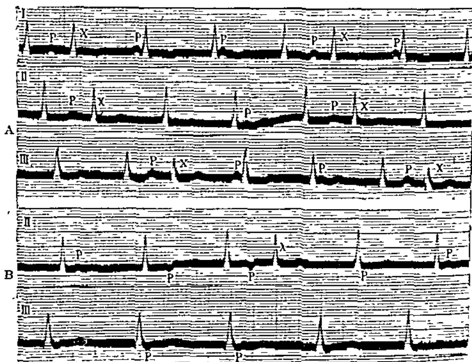


FIG 46

A —*Interference* dissociation Note upright P waves at a rate of 64, with a ventricular rate of 100 Early beats (marked X) are clearly seen when P and T summate

B —Reciprocal rhythm L ... upright P in S-T interval ... with inverted P (R-P=0 24 ... by the fourth R (marked X ... complexes show complete dissociation

T wave coincide, since earlier in the cycle the impulse will find the ventricle refractory, while if the sinus impulse comes later the ventricle will have already responded to the next nodal impulse (Fig. 46A). Clinically the irregularity simulates premature auricular beats since there are no compensatory pauses. Changes in the

intensity of the first sound have also been noted. The dissociation lasts a few days only and requires no treatment as the patient will be confined to bed on account of the infection. As he recovers, the patient may pass through stages of reciprocal rhythm, nodal rhythm (Fig. 46B) and latent heart block with prolonged P-R interval, illustrating the nature of the disorder (33).

The opposite condition of retrograde conduction when orthograde conduction is blocked is seen sometimes in complete A-V heart block when inverted P waves deform the S-T interval about 0.16 second after R waves which follow the preceding P by about 0.50 seconds (34) This shows that the auricle has been activated from the ventricle, and may indicate a supernormal recovery phase in the auricle. Mechanical stimulation of the auricle by the ventricular contraction has been advanced as an explanation, but this is unlikely as the inverted P indicates a retrograde spread of the impulse (35).

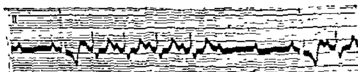


FIG 47

Stokes-Adams Disease Effect of adrenalin Note short runs of normal beat which begin with a premature ventricular systole, and continue until th auricular rate slows

Treatment of Heart Block. *Latent Heart Block* requires n special treatment. Syphilis should be excluded. digitalis ma have to be stopped. But digitalis in therapeutic doses does nc augment heart block due to structural disease. In 16 cases i whom it was pushed to a point of nausea, the P-R interval wa increased slightly in six only, while it was actually reduced in tw following clinical improvement (36).

Partial Heart Block with Dropped Beats is found mainly infections and the patient should be confined to bed. Atropir gr 1/30th–1/75th given intravenously will usually succeed abolishing the heart block temporarily. Caffein sodium benzoa given by intravenous injection in doses of 15 grs, abolished bo the block and Cheyne-Stokes respiration

(37). 2-1 block is often stable for long periods and then requires no treatment.

Complete Heart Block requires no special treatment. Digitalis is not contra-indicated if required to combat congestive failure.

STOKES-ADAMS SYNDROME. The treatment depends upon the underlying cause, which can only be determined accurately by electrocardiograms taken during an attack. When shock is present, as in coronary occlusion and diphtheritic myocarditis, it is important to keep the patient warm. *Adrenalin, m.x* of 1 in a 1,000 solution should be given subcutaneously to prevent ventricular standstill (Fig. 47). An intracardiac injection may be needed if the ventricle has ceased to beat. Some cases respond better to atropine, gr. 1/30th given intravenously. Leptazol in doses of 1cc. given subcutaneously or a tablet every hour succeeded in two cases when adrenalin and atropine has failed (38). Amyl nitrite controlled the attacks in one case with intermittent heart block (39).

Adrenalin is also useful in faintness due to a slow idio-ventricular rhythm. Premature ventricular systoles may be stimulated, followed by spells of normal rhythm (Fig. 47).

To prevent recurrence of attacks ephedrine, gr. ½, four times daily, or paredrine, 10 to 60 mg. thrice daily (40) may be taken indefinitely. Intolerance is shown by nausea, indigestion or palpitation.

For attacks due to ventricular fibrillation or tachycardia quinidine must be given by intravenous injection (p. 300).

The Course and Prognosis of A-V Heart Block. This depends upon the nature of the lesions which have caused it. In acute lesions, such as a septal infarct or diphtheritic myocarditis, the immediate prognosis is bad. Stokes-Adams attacks are common, and they frequently prove fatal. But if the patient survives these, the conduction of the impulse in due course becomes normal. *Heart block in rheumatic carditis, even if complete,* is seldom dangerous, but recovery is often incomplete, some lengthening of the auriculo-ventricular conduction time persisting.

Heart block associated with chronic fibrotic lesions in elderly people is usually permanent, but minor grades of latent heart block are of little or no importance. Even *complete heart block* is

compatible with fair activity for years: and the prognosis depends upon the state of the myocardium as a whole. Some patients die eventually from congestive failure but the majority die suddenly. When complete or partial heart block is associated with variable bundle branch block complexes, bilateral bundle branch lesions are probably present and the prognosis is bad. Stokes-Adams attacks are liable to recur and the patient usually dies in an attack within a year or so.

Bundle Branch Block

The recognition of bundle branch block is important in order to interpret correctly certain abnormal forms of QRS which may indicate a local defect, and because a local defect may point to the presence of lesions elsewhere in the silent areas of the myocardium.

The curves of bundle branch block are caused through the delayed activation of one ventricle and the prior activation of the other. The diagnosis can only be made by means of electrocardiograms, although confirmatory evidence can be obtained at *times* by a lack of synchronism in the contraction of the ventricles. It has been thought that the reduplication of the first sound in gallop rhythm might indicate this asynchronism, there is actually no constant association; *the fact is that* both gallop rhythm and bundle branch block are commonly found in hypertensive heart disease: but with a rate under 90 bundle branch block may be suspected.

Aetiology. Eighty per cent of cases are due to coronary artery disease in later life, the average age at which the lesion is diagnosed being 59 (41). This includes cases of infarction, of which 15 per cent involve the septum (42). Rheumatic heart disease accounts for 10 per cent, the *remainder* being due to syphilis, diphtheria or congenital lesions. It is doubtful if the vagus has any influence over conduction in the bundle branches.

Morbid Anatomy. Histological examination of the bundle branches in cases of bundle branch block have shown that the lesions are usually bilateral, although one branch may be more seriously affected than the other (43). Fibres arising above and just below the bifurcation of the bundle have been traced into the

ventricular muscle (44). When both branches are destroyed, the impulse may reach the ventricles through these fibres.

Glomset (2), who was unable to find satisfactory evidence of a special conducting system in the ventricles, offers another explanation for bundle branch block. It has been shown that the ventricle on the diseased side contracts later than the healthy ventricle. He considers that this ventricular lag is the cause of the electrocardiographic changes and that bundle branch block is due either to an unilateral ventricular strain or to an unilateral ventricular coronary insufficiency, or to a combination of both. Among other difficulties in accepting this view are those cases in which the bundle branch complexes change abruptly from one side to the other in the course of a record. Moreover, Robb has obtained bundle branch block when the lateral mass of the ventricle was cut away and only the septum remained (45). Even if the bundle branches are shown eventually to be nothing more than muscle fasciculi, it seems certain that there is some path of conduction by which each ventricle receives the impulse from the nerve elements in the auriculo-ventricular groove.

Electrocardiograms in Bundle Branch Block. Increased Duration of the QRS. The normal duration of the QRS is about 0.08 second. In bundle branch block it is always increased: usually from 0.12 to 0.16 second, and in some cases up to 0.20 second. Some difference of opinion exists regarding the meaning of curves with smaller increases in the QRS. Lewis (1925) considered that all cases with QRS values above 0.10 second had bundle branch block, and this view has been followed by the authors of several recent series (46), (47). On the other hand Wilson (48) found that when the QRS was less than 0.12 second, chest leads were not usually consistent with complete left bundle branch block though they might be with right. A greatly enlarged left ventricle may take more time to be fully activated than one of normal size, and this will account for a moderate increase in the duration of the QRS. Apart from cases with left ventricular hypertrophy a QRS above 0.10 second probably always indicates bundle branch block of some degree.

Precordial Leads. *The Intrinsic Deflection.* When experimentally a lead is placed directly on the epicardium, a negative deflection is recorded on the galvanometer when the main ventri-

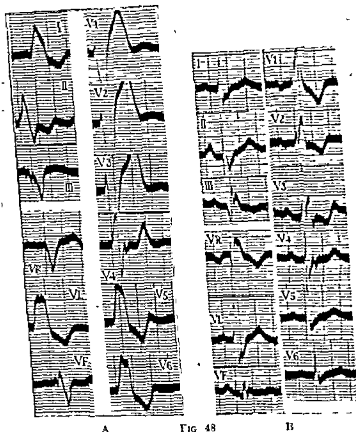


FIG 48

A—Left bundle branch block The heart is horizontal Note early intrinsic deflection in leads V1 and V2 and delayed intrinsic deflection in V5 and V6

B—Right bundle branch block Wide S, pattern The intrinsic deflection is late in V1 to V3 and early in V4 to V6

cular mass under the electrode is activated. This was named by Lewis the intrinsic deflection, and it is always negative. The same deflection occurs in precordial leads and constitutes in bundle branch block the only certain evidence as to the side of the lesion. In left bundle branch block a deep S or QS occurs early in leads taken from the right side of the precordium (V1 and V2), whereas in those from the left side (V5 and V6), the descending arm of the broad R is delayed by 0.10 second or more (Fig. 48A). In right

ventricular muscle (44). When both branches are destroyed, the impulse may reach the ventricles through these fibres.

Glomset (2), who was unable to find satisfactory evidence of a special conducting system in the ventricles, offers another explanation for bundle branch block. It has been shown that the ventricle on the diseased side contracts later than the healthy ventricle. He considers that this ventricular lag is the cause of the electrocardiographic changes and that bundle branch block is due either to an unilateral ventricular strain or to an unilateral ventricular coronary insufficiency, or to a combination of both. Among other difficulties in accepting this view are those cases in which the bundle branch complexes change abruptly from one side to the other in the course of a record. Moreover, Robb has obtained bundle branch block when the lateral mass of the ventricle was cut away and only the septum remained (45). Even if the bundle branches are shown eventually to be nothing more than muscle fasciculi, it seems certain that there is some path of conduction by which each ventricle receives the impulse from the nerve elements in the auriculo-ventricular groove.

Electrocardiograms in Bundle Branch Block. Increased Duration of the QRS. The normal duration of the QRS is about 0.08 second. In bundle branch block it is always increased: usually from 0.12 to 0.16 second, and in some cases up to 0.20 second. Some difference of opinion exists regarding the meaning of curves with smaller increases in the QRS. Lewis (1925) considered that all cases with QRS values above 0.10 second had bundle branch block, and this view has been followed by the authors of several recent series (46), (47). On the other hand Wilson (48) found that when the QRS was less than 0.12 second, chest leads were not usually consistent with complete left bundle branch block though they might be with right. A greatly enlarged left ventricle may take more time to be fully activated than one of normal size, and this will account for a moderate increase in the duration of the QRS. Apart from cases with left ventricular hypertrophy a QRS above 0.10 second probably always indicates bundle branch block of some degree.

Precordial Leads. *The Intrinsic Deflection.* When experimentally a lead is placed directly on the epicardium, a negative deflection is recorded on the galvanometer when the main ventri-

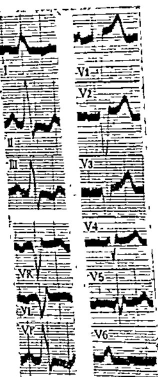


FIG 49
Left bundle branch block with vertical heart Standard leads are of the concordant type

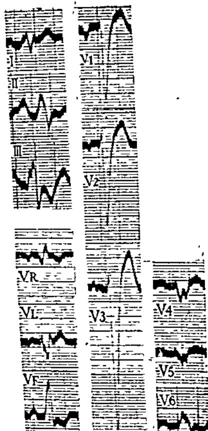


FIG 50
Left bundle branch block with vertical heart.

bundle branch block the left ventricle is enlarged and the position of the heart is either normal or transverse. VL will then represent the potentials of the left ventricle and have positive deflections. The polarity of VL is reversed in lead I and lead III, since lead I is VL-VR and lead III is VF-VL (p. 124). When VL has positive deflections discordant curves will result in the standard leads.

If the heart is vertical the potentials from the left ventricle are transmitted to the left leg and those of the left arm are either small or negative. In these cases the deflections in lead III will be

branch block V1 and V2 have a broad R, the descending arm of which is the intrinsic deflection, while in V5 and V6 there is a slender R with an early downstroke, showing prior activation of the left ventricle, followed usually by a broad but shallow S (Fig. 48B).

POSITION OF THE HEART. Standard lead curves in bundle branch block may be discordant; that is the deflections in lead I are opposite in direction to those in lead III; or concordant. These types are found only in the standard leads, have no counterpart in the precordial leads, and are due to varying positions of the heart.

Unipolar Limb Leads. The aorta and pulmonary artery, as they arise, point towards the right shoulder. When the heart is in a normal position, therefore, the right arm lead (VR) reflects the electrical state of the ventricular cavities (48). Tracings taken from the right auricle and ventricle by means of an electrode fitted into a cardiac catheter have shown that the deflections in VR resemble those at the upper part of the right auricle, and seem to represent a mixture of the potentials of the two ventricles (49). Since the ventricular cavities are negative during activation of the ventricles, the deflections in lead VR are normally inverted. When the position of the heart is normal the deflections in the left arm lead (VL) and the left leg lead (VF) are [illegible] s reflect the pot[illegible] the left arm [illegible] and the left leg the diaphragmatic [illegible] posterior surface. Should there be a clockwise rotation of the heart causing it to be more vertical than usual, the great vessels will tend to point directly upwards, or mid-way between the right and left shoulders. In this case the deflections from the left arm (VL) will resemble those of the right arm and be negative. The left leg will reflect the state of the left ventricle, and the deflections will be positive and similar to those obtained from leads over the left side of the chest (V5 and V6) (Fig. 49). If the rotation is anti-clockwise, causing the heart to be more transversely placed than normal, the great vessels, as they arise, will point between the right arm and the left leg. In that case VF will resemble VR, having negative deflections, while VL will reflect the state of the left ventricle and have positive deflections similar to those in V5 and V6. In the majority of cases of left

Right Bundle Branch Block. PRECORDIAL LEADS. Precordial leads are especially necessary in right branch block, partly because of the variability in the standard leads, and partly because of the great influence of changes in the position of the heart.

In right branch block, leads from the right side differ greatly from the normal. A broad, notched R, the descending limb of which may be delayed by as much as 0.16 second, is seen in V1, and usually also in V2 and V3 (Fig 51). There may be a small primary R followed by a small S. A prominent Q in these leads suggests infarction of the septum (p 205). In leads from the left side a slender R is seen, the downward limb indicating the early activation of the left ventricle. This wave is usually followed by a broad shallow S. These changes are pathognomonic of a right-sided lesion.

LEADS I, II, III. The curves of right branch block in the standard leads are very variable. In one type there is in lead I an initial deflection (S) which is deep, broad and negative and is followed by an upright T. In lead III a broad, upward positive deflection (R) is followed by an inverted T. This type is the converse of that of left bundle branch block. Actually it is rare, and by far the greater number of right branch block curves are of the *wide "S wave" type* (53). In lead I a slender, though tall, initial deflection (R) is

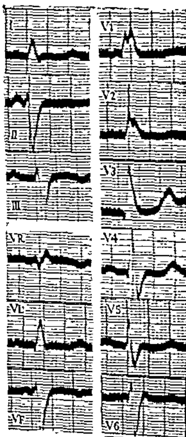


FIG 51

Right bundle branch block. Note intrinsic deflection is delayed on right of by 0 16 second and is early on left Complete heart block

positive and the curves will be concordant. When rotation is extreme and the deflections in lead VL are negative, standard lead curves suggesting right branch block may be shown by precordial leads to be due to a lesion of the left branch (Fig. 50).

Thus classifications based on discordant and concordant types are without value, the variations being due to alterations in the position of the heart. To be sure of the side of the lesion it is necessary to take multiple precordial leads.

Ventricular Asynchronism. By means of simultaneous optical records of the apex beat, the venous and subclavian pulses, it is possible to determine if one ventricle contracts before the other. In 15 out of 17 cases of left branch block the right ventricle was shown to contract first, but in only one out of 3 cases of right branch block did the left ventricle contract before the right (50). This discrepancy may have been due to an abnormality in the lie of the heart, which affected the curves, for in some types of right branch block it was found that delay might occur in either ventricle (51).

Left Bundle Branch Block. The curves of left bundle branch block recorded by the standard leads have in lead I an initial deflection (R) which is high, broad, notched and positive. S waves are not found; Q waves are rare, being present only in 8 per cent and suggest previous infarction of the septum (52). The T wave is usually inverted but may be upright.

Lead II is variable. deflections are often small but an R or S of different dimensions may be found. In lead III a broad, notched, negative S is followed by an upright T, if the heart is in a normal or horizontal position. In vertically placed hearts the complexes are similar to those in leads I and II.

Precordial Leads. In leads over the right side the normal R is either absent or very small and a deep S occurs at once, or very early, showing that the right ventricle is receiving the impulse first. In leads over the left side a broad, notched R is seen, the descending arm of which marks the late activation of the left ventricular muscle. On account of the variable width of the transitional zone in bundle branch block, this feature may not appear until V6. This happens especially when the heart is vertical. (Fig. 49, 50).

QRS in lead I is di- or tri-phasic, however small the Q or S wave may be (48) But confirmation should be sought in the precordial leads.

Bilateral Bundle Branch Block. Not every case with a broadened QRS has a precordial series typical of an unilateral lesion. After an infarct or administration of quinidine, the conduction of the QRS may exceed 0.12 second, and yet precordial leads may not be characteristic of a complete branch block. In these a general depression of the Purkinje tissue has been postulated (48). Again in certain cases with established A-V heart block ventricular deflections characteristic of both right and left branch block alternate In some of those it seemed likely that conduction was taking place alternately down each branch (27). In one case with normal A-V conduction the P-R interval increased by 0.05 second when the branch block changed from left to right (54) Since the P-R interval includes the time taken by the impulse to pass along the bundle branches, until the activation of the first elements of ventricular muscle, it seemed as if conduction was normally through the right branch. When this failed, conduction was maintained by the left branch with an added delay of 0.05 second. It may be also that bilateral lesions are present when the QRS is of very long duration, some of the prolongation being due to the slow passage of the impulse along the lower portion of the less diseased branch.

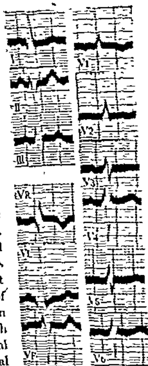


Fig 53

Incomplete right branch block Note small R waves with delayed 'intrinsic deflection on right side QRS 0 10 second There is left axis deviation and the heart is horizontal From a patient with hypertension and Paget's disease.

Incomplete Bundle Branch Block. When the delay in the passage of the impulse down a bundle branch is insufficient to allow of the complete activation of the affected ventricle through the septum, incomplete bundle branch block is said to be present.

followed by a broad, but shallow, negative deflection (S). The T is positive. In lead III the complexes are variable. A broad positive deflection (R) may be followed by an inverted T. A slender negative deflection (S) may be followed by a second broad positive deflection (R_1), the T being negative. In a small proportion of cases R is absent and a deep S is followed by a positive T.

Thus it is apparent that the only definite changes are found in lead I. Right branch block should always be suspected when the



Fig 52

17 1 44 Incomplete right branch block (QRS 0 10 second) showing restoration of normal rhythm

Lead I Nodal rhythm at rate of 100 No evidence of auricular activity

Lead II Nodal rhythm P waves deform S-T interval of alternate complexes

Lead III P waves move forward from S-T till SA node takes control at fifth complex when *QRS returns* to normal

24.2 44
but trans

QRS in lead I is di- or tri-phasic, however small the Q or S wave may be (48) But confirmation should be sought in the precordial leads.

Bilateral Bundle Branch Block. Not every case with a broadened QRS has a precordial series typical of an unilateral lesion. After an infarct or administration of quinidine, the conduction of the QRS may exceed 0.12 second, and yet precordial leads may not be characteristic of a complete branch block. In these a general depression of the Purkinje tissue has been postulated (48). Again in certain cases with established A-V heart block ventricular deflections characteristic of both right and left branch block alternate. In some of those it seemed likely that conduction was taking place alternately down each branch (27) In one case with normal A-V conduction the P-R interval increased by 0.05 second when the branch block changed from left to right (54). Since the P-R interval includes the time taken by the impulse to pass along the bundle branches, until the activation of the first elements of ventricular muscle, it seemed as if conduction was normally through the right branch. When this failed, conduction was maintained by the left branch with an added delay of 0 05 second. It may be also that bilateral lesions are present when the QRS is of very long duration, some of the prolongation being due to the slow passage of the impulse along the lower portion of the less diseased branch.

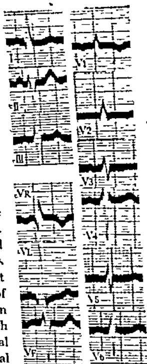


FIG 53

Incomplete right branch block Note small R waves with delayed intrinsic deflection on right side QRS 0 10 second There is left axis deviation and the heart is horizontal From a patient with hypertension and Paget's disease

Incomplete Bundle Branch Block. When the delay in the passage of the impulse down a bundle branch is insufficient to allow of the complete activation of the affected ventricle through the septum, incomplete bundle branch block is said to be present.

There may be a double activation of the affected ventricle, *partly* from its own side and partly from the other, or else the ventricle on the healthy, or relatively healthy, side may merely receive the impulse first. The QRS duration in these cases does not usually exceed 0.10 second, and it may be less. It is then impossible to make the diagnosis unless there are normal complexes in the same record for comparison (55) (Fig. 52A). In some cases the transition from bundle branch block to normal conduction is gradual, the intermediate complexes being those of incomplete block (56). In incomplete right branch block the precordial leads over the right side have a peculiar form, an initial Q wave being followed by a late R wave, which is small or embryonic (48) (Fig. 53).

Precordial leads of incomplete left branch block cannot be distinguished from left-sided hypertrophy with increase in the duration of the QRS.

Incomplete bundle branch block is probably quite common. It is seen in the aberrant ventricular complexes following auricular premature systoles (57). But there are few satisfactory criteria for diagnosis in the absence of normal complexes at some time for comparison (Fig. 52B).

Partial Bundle Branch Block is analogous to partial A-V heart block with dropped beats, and is rare. Every other complex may show bundle branch block (2-1 branch block) or every third: or two complexes of branch block may alternate with one normal complex (3-1) (58). Or an occasional normal beat may be seen in a record of predominantly bundle branch block complexes. In INTERMITTENT BUNDLE BRANCH BLOCK occasional complexes of bundle branch block are found in a record of mainly normal complexes.

TRANSIENT BUNDLE BRANCH BLOCK. Bundle branch block usually persists, but is sometimes transient. Recovery is the rule in the myocarditis of diphtheria, if the patient survives the acute phase. In acute rheumatism, and after septal infarcts conduction recovers less often

Apart from these causes, phases of bundle branch block may be associated with acute myocardial strain such as follows a pulmonary embolism (59). Temporary bundle branch block lasting from a few days to months may be associated with periods of congestive failure. In these cases conduction down one branch is

probably delayed almost to the point at which the impulse will reach the affected ventricle quicker by the other branch and across the septum, and an increase in heart rate alone may be sufficient to cause branch block complexes to appear (60). Carotid sinus pressure, by slowing the rate, may restore normal conduction (61). Occasionally no obvious cause can be found to account for the changes in conduction (62). In one case of bundle branch block atropine given intravenously caused a tachycardia, and led to partial 2-1 branch block. The tachycardia probably made the damaged branch completely refractory to the blocked impulses, and so it was able to transmit the alternate ones (63).

Course and Prognosis. Bundle branch block itself does not interfere with the efficient working of the heart. As it is due to a local myocardial lesion of greater or less severity, it is upon the cause, and the extent of the associated disease that the prognosis depends. In 80 per cent of all cases the heart is enlarged: in 60 per cent congestive failure or angina pectoris was present when the branch block was detected (46), so that it is not surprising that about one-third of all cases die within a year of the discovery of the lesion (64). Yet although the average age at which branch block is first found is comparatively high, one quarter live 10 years or more (65). Right branch block has a better prognosis than left (66) This is probably due to the inclusion of the wide "S-wave" type, which has the best prognosis of the common varieties, 38 per cent living ten years. This good outlook was only shared by 16 per cent of those with standard right or left branch block curves, and by 26 per cent of those with atypical curves (65).

Short P-R Interval and Bundle Branch Block Type of QRS. (Wolff, Parkinson, White Syndrome). Complexes suggesting bundle branch block may be found associated with a P-R interval of less than 0.12 second. In these cases one ventricle is probably activated first through an accessory branch of the A-V bundle (Bundle of Kent) which constitutes a short cut (67). Ohnell (68) has discussed the condition in an exhaustive monograph, and describes an accessory bundle to the left ventricle from the left auricle Curves show, as a rule, left bundle branch block the right ventricle, therefore, receives its impulse first because there is a shorter path to it and not because there is a delay in the passage of the impulse to the left ventricle The



Fig 54
Wolff-Parkinson-White syndrome Lead I, P-R interval is 0.08 sec QRS is 0 14 sec

abnormality may be permanent, or may alternate with periods of normal conduction (69). Paroxysms of auricular or ventricular tachycardia may occur in these patients (70). These have been fatal (68). Otherwise the condition is benign and does not signify myocardial disease and has really nothing to do with bundle branch block. But it must be distinguished from it (Fig. 54).

REFERENCES

1 Glomset, Glomset (1940) *Amer Heart J*, **20**, 677
2 Glomset, Glomset Birge (1944). *Amer Heart J* **28**, 348
3 Rosenbaum, Levine (1939) *Amer J. med Sci*, **198** 774
4 Cavinnes (1943) *Amer Heart J*, **25**, 128
5 Scherf Harris (1946) *Amer Heart J*, **32**, 443
6 Parkinson, Papp, Evans (1941) *Brit Heart J*, **3** 171
7 Eichna, Horvath, Bean (1947) *Amer Heart J*, **33**, 254
8 Mayerson (1943) *Amer J Physiol* **138**, 630
9 Graybeil, White (1936) *Amer J med Sci*, **192**, 334
10 Bruenn (1937) *Amer Heart J*, **13**, 413
11. Perry (1939) *Brit Heart J*, **1**, 117
12. Steler (1936) *Amer Heart J*, **11**, 623
13. Bain (1945) *Brit Heart J*, **7**, 49
14 Geiger Hines (1940) *J Amer med Ass*, **115**, 2272
15 White, Leach Foote (1941) *Amer Heart J*, **22**, 320
16 Reyersbach, Kuttner (1940) *Amer Heart J*, **20**, 573
17 Holmes, Weill (1945) *Amer Heart J*, **30**, 291
18 Campbell (1943) *Brit Heart J*, **5** 163
19 Campbell (1942) *Brit Heart J*, **4**, 131
20 Campbell (1943) *Brit Heart J*, **5**, 55
21 Parsonnet Miller (1944) *Amer Heart J* **27** 676
22 Yater, Cornell, Clayton (1936) *Arch intern Med*, **57**, 132
23 Hutchinson, Reed (1942) *Amer Heart J*, **24**, 113
24 Comeau (1937) *Amer J med Sci* **194**, 43
25 Kline, Conn, Rosenbaum (1939) *Amer Heart J*, **17**, 524
26 Schwartz (1936) *Amer Heart J*, **11**, 554
27. Bain (1941) *Brit Heart J*, **3**, 75
28 Pearson (1945) *Brit Heart J*, **7**, 85
29 Sigler (1938) *Amer Heart J*, **16**, 109
30 Bain (1938) *Lancet*, **1**, 26
31. Cutts (1938) *Amer Heart J*, **14**, 717.
32. Cutts (1937) *Amer Heart J*, **13**, 451
33 Bain (1939) *Lancet*, **1**, 20
34 Winternitz, Langendorf (1944) *Amer Heart J*, **27**, 301
35 Kisch, Zucker (1942). *Amer Heart J*, **23**, 269.

Sci, 198, 445
296

Heart J., 24, 153
J, 67, 1027
16, 283

rt J, 25, 251.
45 Robb, Robb (1942) *Amer J med Sci*, 204, 313
46 Willius, Dry, Reeser (1941). *Arch intern Med*, 67, 1008
47 Kaplan, Katz (1939) *Amer Heart J*, 18, 145
48 Wilson, Johnston, Rosenbaum, Erlanger, Kossmann, Hecht, Hecht, Cotrim, De Oliveira, Scarsi, Barker (1944). *Amer Heart J*, 27, 19
49 Hecht (1946) *Amer. Heart J*, 32, 39
50 Braun-Menendez, Solari (1939) *Arch intern Med*, 63, 830
51 Bohning, Katz, Langendorf, Blumenthal (1941). *Amer J. med Sci*, 202, 671
52 Sodeman, Johnston, Wilson (1944) *Amer Heart J.*, 28, 271.
53 Bayley (1935) *Amer J med Sci.*, 188, 236

3

4

Abnormality,
Stockholm
69 Hunter, Papp, Parkinson (1940) *Brit Heart J*, 2, 107.
70 Levine, Beeson (1941) *Amer Heart J*, 22, 401

Postural (Orthostatic) Hypotension. This rare derangement of the control of the pressure in the arterial system has aroused some interest since first described in 1925 (1). A peculiar result of a nervous disease, it is awkward to fit into any classification, but as a persistently slow rate and syncope are conspicuous features, this chapter seems the best place for it.

On standing up the patient feels faint and giddy and may collapse. The unpleasant nausea of the vaso-vagal attack is lacking. The blood pressure falls profoundly. On lying down it reaches the level normal for him. The symtoms are most pronounced in the morning The fall in arterial pressure on standing up is almost entirely confined to males, and comes on about

middle age. Nearly all cases show two other important, but less spectacular, symptoms, namely loss of sweating and impotence This triad, as one may term it (2), points to some lesion in the central nervous system as a cause. Quite a large proportion of the patients have tabes dorsalis, or syringomyelia, or they have had an attack of encephalitis (3).

The nature of the loss of control of the arterial blood pressure has been investigated by Stead and Ebert (4), who found that there was not an abnormal degree of pooling of the blood in the lower part of the body on standing up, but rather a failure to make adjustments to allow for the pooling of a normal quantity. If the patient stood in water up to the heart the blood pressure did not fall. If the patient is tilted head downwards the brachial pressure rises. Valsalva's experiment by reducing the venous return to the heart causes a sharp fall in arterial pressure. There is not the usual decrease in the flow of blood in the fingers in these patients, which takes place when a healthy person stands up; this shows lack of vaso-constriction (5). The muscular coats of the arterioles react to pituitrin; adrenalin and the other sympatheticomimetic drugs cause the pressure to rise. The response to adrenalin may be much greater than normal, causing much acceleration and a great rise in pressure (2)

The rate of the heart varies but little, as a rule, with changes in posture. After atropine there is little or no acceleration.

Course and Prognosis. The disease, when established, persists almost invariably; only one remission has been recorded. Once it has reached a certain degree it does not appear to get worse, and no fatal cases are on record.

Treatment. This is not satisfactory and can only be palliative. Sleeping with the head of the bed raised may render the fall in pressure less. Binders do not help much. The vaso-constrictors such as ephedrine (30 mg.) and paredrine (30 mg.) are useful in the later part of the day, and benzedrine (5 0 mg. every hour) may be of distinct value in the mornings In one case sweating returned and impotence ceased after the administration of 100 mg. benzedrine in the mornings and 160 mg. of paredrine in the afternoons (6).

The further elucidation of this disturbance in the control of the arterial pressure awaits study of the central nervous system. So far no autopsies have been recorded.

REFERENCES

1 Bradbury, Eggleston (1925) *Amer Heart J*, 1, 73.
2 East, Brigden (1946) *Brit Heart J*, 8, 103
3 Woofter, Deibert (1943) *Amer. J syph ven dis*, 27, 616
4 Stead, Ebert (1941) *Arch intern med*, 67, 546
5 Jeffers, Montgomery, Burton (1941) *Amer J med Sci*, 75, 336.
6 Korns, Randall (1938) *Ann intern Med*, 12, 253

CHAPTER IX

TACHYCARDIA

Sinu-Auricular Tachycardia

Auricular Premature Beats: Paroxysmal Tachycardia: Auricular Fibrillation and Flutter

Ventricular Premature Beats: Paroxysmal Tachycardia and Fibrillation

It is not usual to consider together all the subjects which come under review in this chapter. There are, however, considerable advantages in doing so. As far as the causation of these disorders is concerned, there is reason to suppose that they have much in common. In the auricles it is well known that auricular premature systoles are closely connected with auricular paroxysmal tachycardia and they may be followed by auricular fibrillation. Fibrillation and flutter are, in a sense, interchangeable, Both are caused by a circulating wave in the auricles. It is possible that some cases of auricular paroxysmal tachycardia are also due to a circulating wave which includes in its ambit either the sinu-auricular or the auriculo-ventricular node. In the ventricles premature systoles and ventricular tachycardia are associated, and ventricular fibrillation is often preceded by bouts of either. Apart from isolated premature beats, the effect of all of them on the efficiency of the heart depends upon the liability to induce a great increase in rate, and thereby provoke failure of the circulation. In their treatment there are many points common to all; particularly in the use of quinidine, and, to a lesser degree, of digitalis.

Sinu-Auricular Tachycardia. This is sometimes called physiological tachycardia since it is not due to any abnormal rhythm in the heart. It occurs in a variety of conditions, of which only a minority are associated with disease of the heart.

MYOCARDIAL FAILURE. Tachycardia occurs in heart failure. The stroke volume diminishes, so the rate may increase in order to maintain the minute volume (1). But the mechanism is by no means clear. As the contraction of the heart becomes more efficient with treatment, the rate slows.

PERIPHERAL CIRCULATORY FAILURE. In shock the volume of venous blood returning to the heart is diminished and the rate of the heart increases in order to attempt to maintain the output. (See Chapter XIII.) The reason for this is obscure.

INFECTIONS. It is well known that in fever the pulse rate rises about ten beats for each degree of rise in temperature. Sometimes the tachycardia is out of proportion to the temperature. In 100 such cases acute myocardial lesions were found in 80 (2). They comprised infarcts, rheumatic heart disease, pericarditis, acute myocarditis. Peripheral circulatory failure, associated with a low blood pressure, is also the cause of the disproportionate tachycardia which occurs in some cases of pneumonia. In a few fatal cases of poliomyelitis in which tachycardia had been a prominent feature an unexpected myocarditis was found (3).

Tachycardia may occur if sufficient rest has not been allowed after an acute infection; this may lead to the development of a cardiac neurosis, which may cause the tachycardia to persist.

HYPERTHYROIDISM causes a persistent tachycardia. The subject is discussed in Chapter VI.

ANXIETY NEUROSIS. Tachycardia is frequently found in anxiety. The patient complains of palpitation: other symptoms are: breathlessness, fatigue, left submammary pain and dizziness. Sweating in the axillæ, and of the palms of the hands and soles of the feet is common, but is found in other patients. Moderate exercise increases the rate but little, and in some cases it may even fall during the first few minutes after the exercise. The syndrome originally described by Da Costa, is mainly due to fear, and results from overaction of the sympathetic (4). There is usually a family history of psychoneurosis, and the patients have been timid since childhood. In others [illegible]

of the hear[illegible]

murmur, an[illegible]

Often there is poor physique both in bone and in muscle. In the 1914-1918 war the name of "Effort S[illegible]

these cases. In civil life the syndrome occurs more commonly in women, and the investigation of the hidden conflict of anxiety neurosis, which is expressing itself in tachycardia will often require the assistance of a psychologist; but simple re-assurance that the heart is not at fault may relieve the anxiety.

GLUCOSE DEFICIENCY. In some cases symptoms occur only two or three hours after meals. They comprise tachycardia, choking pain in the chest, tremor, muscular weakness, and occasionally fainting. The attacks can be reproduced by injections of 10 to 15 units of insulin three hours after a meal; they can be relieved by glucose. The blood *sugar at the time of the attack is either low* or has a low normal value; the glucose tolerance curve falls sharply. The symptoms are probably due to the release of adrenalin to combat the falling blood sugar. They are best treated by a high protein and low carbohydrate diet, which does not cause so much insulin to be secreted. Intermediate feeds are also useful (5). Some rare cases are on record in which there was a combination *of severe tachycardia and postural hypotension (6).* Hyperinsulinæmia due to tumour of the islets of Langerhans must be remembered.

Premature Systoles

Premature systoles may arise from the auricles, the A-V node, or from the ventricles. Exceptionally they may come from the S.A. node (7). *The irritable point in the heart muscle initiates a* contraction before the normal impulse from the sinu-auricular node has reached it.

A premature beat is weak, as the ventricle is incompletely filled at the moment of contraction. The beat may, or may not, open the aortic valves, and cause a wave to be transmitted to the pulse. Clinically premature beats are recognisable by the irregularity of the pulse. *Either the pulse is intermittent, a beat* being dropped, or else a weak and early beat can be felt. The succeeding normal beat—the returning beat—is usually stronger than normal. The premature contraction can be heard at the heart, except in rare instances of blocked auricular premature systoles, and the diagnosis is best made by auscultation, in order to differentiate this irregularity from true dropped beats of heart block. Beats that fail *to cause a pulse wave may only give the*

first heart sound for the valves will not open. Otherwise both sounds are present: those that occur very early in diastole may be very faint.

Premature systoles are not common when the rate of the heart is over 110 a minute, so acceleration of the heart by exercise may abolish them. When they are present at this rate the muscle is usually diseased.

Auricular Premature Systoles. The P wave in the electrocardiogram is premature; it may be inverted, biphasic, or of a size different from that of the other P waves in that lead (Fig 55), or be superimposed upon the preceding T wave. The variations from the normal are best seen in leads II and III, or in chest leads reflecting the potentials of the right side such as V1 or V2. In most

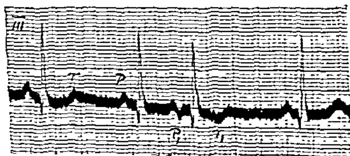


FIG 55.
An auricular extrasystole P_1 Note that the T wave of the subsequent ventricular complex is inverted, "aberration"

cases th...
to the
direct ... (b). The extent of the aberration depends
upon the de...
inc
do ... the only factor, as aberration may be
increased for a time after quinidine or during ...

is then no ventri... the impulse is blocked, and there

these cases. In civil life the syndrome occurs more commonly in women, and the investigation of the hidden conflict of anxiety neurosis, which is expressing itself in tachycardia will often require the assistance of a psychologist; but simple re-assurance that the heart is not at fault may relieve the anxiety.

GLUCOSE DEFICIENCY. In some cases symptoms occur only two or three hours after meals. They comprise tachycardia, choking pain in the chest, tremor, muscular weakness, and occasionally fainting. The attacks can be reproduced by injections of 10 to 15 units of insulin three hours after a meal; they can be relieved by glucose. The blood sugar at the time of the attack is either low or has a low normal value; the glucose tolerance curve falls sharply. The symptoms are probably due to the release of adrenalin to combat the falling blood sugar. They are best treated by a high protein and low carbohydrate diet, which does not cause so much insulin to be secreted. Intermediate feeds are also useful (5). Some rare cases are on record in which there was a combination of severe tachycardia and postural hypotension (6). Hyperinsulinæmia due to tumour of the islets of Langerhans must be remembered.

Premature Systoles

Premature systoles may arise from the auricles, the A-V node, or from the ventricles. Exceptionally they may come from the S.A. node (7). The irritable point in the heart muscle initiates a contraction before the normal impulse from the sinu-auricular node has reached it.

A premature beat is weak, as the ventricle is incompletely filled at the moment of contraction. The beat may, or may not, open the aortic valves, and cause a wave to be transmitted to the pulse. Clinically premature beats are recognisable by the irregularity of the pulse. Either the pulse is intermittent, a beat being dropped, or else a weak and early beat can be felt. The succeeding normal beat—the returning beat—is usually stronger than normal. The premature contraction can be heard at the heart, except in rare instances of blocked auricular premature systoles, and the diagnosis is best made by auscultation, in order to differentiate this irregularity from true dropped beats of heart block. Beats that fail to cause a pulse wave may only give the

Ventricular Premature Systoles cause highly abnormal ventricular deflections of the same kind as in bundle branch block. They are usually large and biphasic. If the main initial deflection is upward, the end deflection is downward; QRS is broadened.

Premature ventricular systoles were formerly divided into those arising from the right and left ventricles on the lines of bundle branch block. Thus an upward initial deflection in lead I with a downward initial deflection in lead III would signify a premature systole arising from the right ventricle just as, if not premature, it would signify left branch block in which the right ventricle is activated first It is doubtful if this view is justified In infarcts the distinction lies between an anterior apical lesion and a posterior basal lesion. In a patient with congenital absence of the lower half of the sternum stimulation of the base of the heart produced premature systoles with upright main deflections in leads II and III, whether the stimulus was applied to the right or the left sides of the heart, while stimulation of the apex resulted always in downward deflections in these leads (9). During an operation for the removal of pleuro-pericardial adhesions in a patient whose heart was rotated, it was possible to stimulate directly the posterior surface of the right ventricle (10) It was found that stimulating the base of the right or left ventricle caused premature systoles with main deflections which were directed downwards in lead I and upwards in lead III, while stimulation of the apex caused upright deflections in lead I and downward in Lead III. Recent experimental work on dogs suggests that the position is complicated (11) Initial upward deflections in lead I, combined with a downward deflection in lead III, signified that the posterior surface of the right ventricle was activated before the anterior surface of the left; upward deflections in both leads I and III indicated that most of the right ventricle was activated before the left. The matter is not yet settled, but it seems that the shape of premature ventricular systoles is determined more by the position of the point at which they arise in relation to the apex or base of the heart than to its location in either ventricle (11). In any case the differentiation of premature ventricular systoles is of little clinical importance. A few years ago the reversal of the formerly accepted interpretation made no difference to diagnosis or prognosis.

In ventricular premature systoles the auricular rhythm is

The impulse from the premature auricular systole passes back to the sinu-auricular node and discharges the one which is forming there. The rhythm of the heart is thus fundamentally disturbed since a new impulse forms at the sinu-auricular node. The pause after an auricular premature systole consists of the normal interval between the beats *plus the time taken by the ectopic impulse to* spread to the S.A. node. It is not so long as the full compensatory pause following ventricular premature beats. Sometimes it is possible to recognise this clinically.

Nodal Premature Systoles. Nodal premature systoles are uncommon. The impulse is generated at the auriculo-ventricular node, and spreads downwards to the ventricles and backwards to the auricles. As in nodal rhythm the P-wave is inverted, and may appear before the QRS, or be buried in it, or follow it. The ventricular complexes are normal.

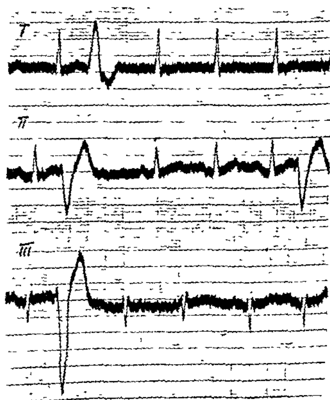


Fig. 56

Ventricular Premature Systoles cause highly abnormal ventricular deflections of the same kind as in bundle branch block. They are usually large and biphasic. If the main initial deflection is upward, the end deflection is downward; QRS is broadened. Premature ventricular systoles were formerly divided into those arising from the right and left ventricles on the lines of bundle branch block. Thus an upward initial deflection in lead I with a downward initial deflection in lead III would signify a premature systole arising from the right ventricle just as, if not premature, it would signify left branch block in which the right ventricle is activated first. It is doubtful if this view is justified. In infarcts the distinction lies between an anterior apical lesion and a posterior basal lesion. In a patient with congenital absence of the lower half of the sternum stimulation of the base of the heart produced premature systoles with upright main deflections in leads II and III, whether the stimulus was applied to the right or the left sides of the heart, while stimulation of the apex resulted always in downward deflections in these leads (9). During an operation for the removal of pleuro-pericardial adhesions in a patient whose heart was rotated, it was possible to stimulate directly the posterior surface of the right ventricle (10). It was found that stimulating the base of the right or left ventricle caused premature systoles with main deflections which were directed downwards in lead I and upwards in lead III, while stimulation of the apex caused upright deflections in lead I and downward in Lead III. Recent experimental work on dogs suggests that the position is complicated (11). Initial upward deflections in lead I, combined with a downward deflection in lead III, signified that the posterior surface of the right ventricle was activated before the anterior surface of the left; upward deflections in both leads I and III indicated that most of the right ventricle was activated before the left. The matter is not yet settled, but it seems that the shape of premature ventricular systoles is determined more by the position of the point at which they arise in relation to the apex or base of the heart than to its location in either ventricle (11). In any case the

In ventricular premature systoles the

undisturbed, but the next impulse from the sinu-auricular node usually finds the ventricular muscle refractory. A "compensatory pause" therefore occurs, the sum of the cycle before the early beat, and that after it, equalling two normal cycles. Occasionally, if the heart is beating slowly, and the ectopic impulse is very early, the ventricle may again be ready to contract by the time the normal impulse arrives. A true extra-systole then results which is spoken of as an "interpolated extra-systole" since the premature systole is interpolated between two normal beats. The P-R interval

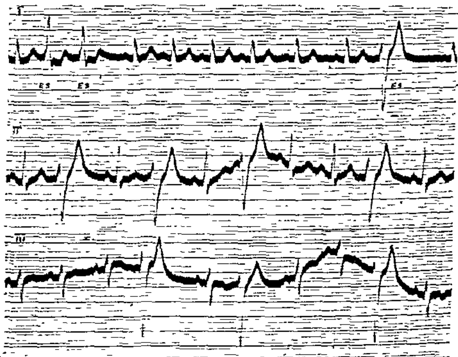


FIG 57
Ventricular premature systoles Arising from two foci

following an interpolated extra-systole is usually prolonged, owing to fatigue in the conducting tissues.

Multiple Premature Systoles may occur, when several ectopic foci are active at the same time. If the rate is rapid, as it often is in these cases, the clinical irregularity may be difficult to distinguish from that of auricular fibrillation.

Ætiology of Premature Systoles. Premature systoles do not by themselves signify heart disease as they are frequently found in

hearts which are otherwise normal. They occur more often in men than in women, and are increasingly common as age advances.

A normal heart may be irritated in a variety of ways. Digestive disturbances, particularly associated with heavy meals, and the excessive use of tea, coffee, tobacco or alcohol may lead to ventricular premature systoles. Injections of adrenalin can produce them, and psychological disturbances may act in the same way through stimulation of the sympathetic nervous system. Premature systoles may arise during the course of any acute infection, or in association with a septic focus.

In myocardial disease premature systoles are often met with in active rheumatism. They appear with ischæmic lesions, and also in acute focal inflammation. In rare cases they are seen in combination with malignant deposits, or in syphilis.

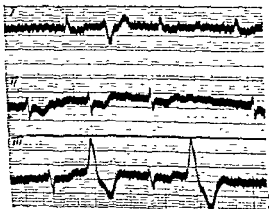


FIG 58
Ventricular premature systoles, due to digitalis effect shown in T2 and T3, in a case with fibrillation

Digitalis produces ventricular premature systoles when it is given in toxic doses. The appearance of a coupled rhythm, in which a ventricular premature systole follows each normal beat, is usually a sign to stop the drug. But coupling may be found to persist sometimes in patients on maintenance doses; then it may be disregarded. There is evidence that premature systoles due to digitalis intoxication may be caused by disturbance in the potassium balance in the heart muscle since they can be abolished by the administration of potassium (19).

undisturbed, but the next impulse from the sinu-auricular node usually finds the ventricular muscle refractory. A "compensatory pause" therefore occurs, the sum of the cycle before the early beat, and that after it, equalling two normal cycles. Occasionally, if the heart is beating slowly, and the ectopic impulse is very early, the ventricle may again be ready to contract by the time the normal impulse arrives. A true extra-systole then results which is spoken of as an "interpolated extra-systole" since the premature systole is interpolated between two normal beats. The P-R interval

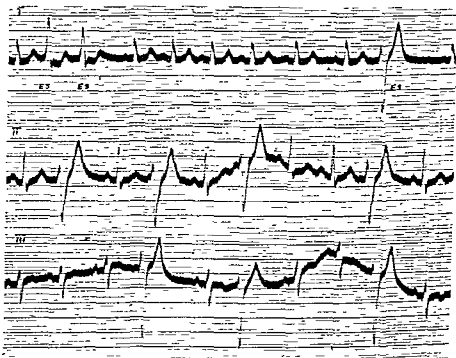


FIG 57
Ventricular premature systoles Arising from two foci

following an interpolated extra-systole is usually prolonged, owing to fatigue in the conducting tissues.

MULTIPLE PREMATURE SYSTOLES may occur, when several ectopic foci are active at the same time If the rate is rapid, as it often is in these cases, the clinical irregularity may be difficult to distinguish from that of auricular fibrillation.

Ætiology of Premature Systoles. Premature systoles do not by themselves signify heart disease as they are frequently found in

occur early in diastole, and would be accurately related in time to the preceding beat. Out of seventy-eight examples of bigeminy due to ventricular premature systoles, fixed coupling of this type was found in forty (15).

Parasystole. The theory of parasystole seeks to explain premature systoles which recur at intervals over long periods. The intervals may be regular or irregular, but if irregular, a common denominator in units of time can be found to cover them all, if a sufficiently long tracing is taken. In these cases there are probably two centres in the heart muscle which are actively producing impulses. The centre with the faster rhythm, which is usually the higher centre, is dominant, but the lower centre is protected from the impulses arising in the higher by an unidirectional block (Entrance Block). Thus there may be a centre in the *ventricle* which is generating impulses at a slower *rate than the dominant* sinus rhythm. It is protected from the normal sinus impulses by the block, but its own impulses can pass out to activate the rest of the ventricle. The heart, however, will not respond to impulses during the refractory period. Only those impulses from the ventricular centre which arrive while the ventricle is receptive, will be answered. The result of this interplay of the two rhythms is that ventricular premature systoles occur at intervals which are usually irregular, since the rate of the lower centre will usually bear no simple mathematical relationship to that of the higher centre. If the rate of impulse formation in the two centres does not alter, however, the intervals between the premature systoles will be related to each other, since the three factors concerned in their appearance—the rate of the higher centre, the rate of the lower centre, and the refractory period of the heart muscle are constant.

Rarely the rate of impulse formation in the ectopic focus is faster than that of the sinus rhythm. In these cases some of the ectopic impulse must also be blocked (Exit Block). In one such case the ectopic focus had a rate of 375 (16).

SYMPTOMS Premature systoles are a cause of discomfort to many people They feel their hearts to be turning over, or else it seems to stop. The strong returning beat after a pause may be felt as an unpleasant thump. On the other hand, less sensitive individuals are often unaware of any irregularity.

PROGNOSIS Multiple

Auricular premature systoles are more often associated with changes in the venous inflow to the auricles. They appear in mitral stenosis and in emphysema. Frequent auricular premature systoles in mitral stenosis may be forerunners of auricular fibrillation.

Nature of Premature Systoles. Single premature systoles can be evoked experimentally by induction shocks, or by means of mechanical or thermal stimuli. Alterations in the quality or quantity of the blood supply may produce them: also stimulation of the autonomic nerves controlling the heart. In certain conditions the heart seems peculiarly liable to generate premature systoles. Thus chloroform may induce a state in which premature systoles may be readily produced by many different stimuli.

"U" Wave and Premature Systoles. The "U" wave is a small, blunt inconstant deflection which follows the T wave. In normal curves it can be recognised only in about 10 per cent of standard leads but in 75 per cent of IVR leads (13). In abnormal curves it is present much less often and may be inverted.

The "U" wave occurs in the same part of the cardiac cycle as the super-normal phase. Most ventricular premature systoles, including those of coupled rhythm, fall on the "U" wave, or begin during that part of the cycle in which it occurs. They, therefore may be related in some way to the super-normal phase, which is known to be increased by asphyxia, acids and some drugs such as chloroform. Less commonly ventricular premature contractions come late in diastole, and these may be due to escapes of the ventricle.

Theory of Re-entry. Another explanation of the coupled rhythm associated particularly with digitalis intoxication is the theory of re-entry. It is suggested that the premature systole is actually produced by the same stimulus as the preceding normal beat (14). The theory is based on the fact that circus movement has been found to involve the ventricles as well as the auricles; and that stimuli applied to partially refractory heart muscle may produce more than one response. It is possible that the original stimulus may find only some fibres able to conduct it, and that the wave may be able to return through other fibres which were at first refractory. In this way a single wave of stimulation could cause a normal beat, and then, by re-entering the ventricle, could excite a second response. The second response would naturally

occur early in diastole, and would be accurately related in time to the preceding beat. Out of seventy-eight examples of bigeminy due to ventricular premature systoles, fixed coupling of this type was found in forty (15).

Parasystole. The theory of parasystole seeks to explain premature systoles which recur at intervals over long periods. The intervals may be *regular or irregular*, but if irregular, a common denominator in units of time can be found to cover them all, if a sufficiently long tracing is taken. In these cases there are probably two centres in the heart muscle which are actively producing impulses. The centre with the faster rhythm, which is usually the higher centre, is dominant, but the lower centre is protected from the impulses arising in the higher by an unidirectional block (Entrance Block). Thus there may be a centre in the ventricle which is generating impulses at a slower rate than the dominant sinus rhythm. It is protected from the normal sinus impulses by the block, but its own impulses can pass out to activate the rest of the ventricle. The heart, however, will not respond to impulses *during* the refractory period. Only those impulses from the ventricular centre which arrive while the ventricle is receptive, will be answered. The result of this interplay of the two rhythms is that ventricular premature systoles occur at intervals which are usually *irregular*, since the rate of the lower centre will usually bear no simple mathematical relationship to that of the higher centre. If the rate of impulse formation in the two centres does not alter, however, the intervals between the premature systoles will be related to each other, since the three factors concerned in their appearance—the rate of the higher centre, the rate of the lower centre, and the refractory period of the heart muscle are constant.

Rarely the rate of impulse formation in the ectopic focus is faster than that of the sinus rhythm. In these cases some of the ectopic impulse must also be blocked (Exit Block). In one such case the ectopic focus had a rate of 375 (16).

Symptoms. Premature systoles are a cause of discomfort to many people. They feel their hearts to be turning over, or else it seems to stop. The strong returning beat after a pause may be felt as an unpleasant thump. On the other hand, less sensitive individuals are often unaware of any irregularity.

Prognosis. Multiple premature systoles from several foci

especially when they are associated with a rapid rhythm, are not found in healthy hearts. Otherwise premature systoles have no prognostic value of their own. Auricular premature systoles have been observed for 24 years without any other abnormality (17). *If there are cardiac lesions, they may have some bearing on the* outlook of the case. In mitral stenosis auricular premature systoles may point to the early onset of fibrillation. After a coronary occlusion ventricular premature systoles somewhat increase the gravity of the prognosis, by suggesting the possible development of ventricular tachycardia (see p. 210).

Single premature systoles do not damage or overload the heart. They may suggest the presence of lesions, but alone they have no more significance than a systolic murmur, or a pulse rate of 120.

Treatment. Premature systoles usually require no treatment, beyond reassuring the patient by telling him that they are of no importance in themselves. Sometimes they may point to a source of toxin which is irritating the heart, and suggest a search for sepsis in the teeth, tonsils, sinuses, gall-bladder, urinary or alimentary tracts. If the premature systoles disturb the patient, the removal of coffee, tea, tobacco or alcohol may be effective in controlling them. Bromide or phenobarbitone may abolish those associated with psychological disturbances. Quinidine sulphate in doses of 10-15 grains daily will often reduce the number of premature systoles materially. Both auricular and ventricular premature systoles can sometimes be checked by the use of small doses of digitalis. Ventricular premature systoles produced by toxic doses of digitalis can be abolished for a time by potassium acetate in doses of five or ten grammes (12). In cases of multiple premature systoles in myocardial disease, or premature systoles occurring in other forms of heart disease, the treatment is that of the associated lesion.

Auricular Fibrillation and Flutter

MECHANISM. It is generally accepted that auricular fibrillation and auricular flutter are caused by a circus movement in the auricles.

LEWIS' THEORY OF CIRCUS MOVEMENT. The impulse from the sinu-auricular node passes down the right auricle and has to surround the openings of the superior and inferior venæ cavæ.

Normally the wave will spread round both sides of each vessel. In this way two waves will be formed which will meet at the further side and mutually extinguish each other. If the muscle at one side should happen to be refractory at the moment the wave started, it could only pass down the other side, and so one wave only would be formed This wave would meet no opposition at the bottom, and there would be nothing to prevent it travelling back to the point from which it started. If the refractory period of the muscle should be less than the time taken by the wave to circulate, a second revolution could be made, and the circus thus started would continue indefinitely.

NATURE OF FLUTTER. In flutter a wave circulates in the auricles with an orbit which includes the orifices of both the superior and inferior venæ cavæ (18). The distance travelled by the wave is comparatively long. The time required for a wave to make a revolution will be greater than that required by the muscle fibres to recover from their absolute refractory period. Although the fibres will still be partially refractory and their conduction time will be slowed, they will be able to respond when the wave reaches them So the impulse goes on and on in its original path.

NATURE OF FIBRILLATION The course of the circulating wave has not been traced in fibrillation It may not be around the great veins Fibrillary waves in the electrocardiograms have a greater frequency than flutter peaks they are also irregular in time and shape. They may fade away in one lead and yet be present in another lead taken simultaneously. These features suggest that the circuit of the wave must be shorter in fibrillation than in flutter. There will not be time for all the fibres to have recovered. The wave will constantly be passing through muscle which is almost wholly refractory. Some fibres will be able to conduct it; others will not The wave will advance through those islands of muscle which are still responsive. It will have to pursue a sinuous course, which will vary at each revolution. Not only will the length of the path alter slightly, but the plane of its axis will be constantly changing.

The difference between auricular flutter and auricular fibrillation lies on the size of the ring In flutter it is *sufficiently* large for a gap to be present between the head of the wave and its tail, where the muscle ceases to be refractory Hence the path of it

constant. In fibrillation the advancing crest is mixed up with the wake. The gap is reduced to a minimum. The wave can only pass along those fibres which happen to be responsive. Its course is, therefore, irregular.

IMPURE FLUTTER is an intermediate stage between flutter and fibrillation. It may occur during the administration of quinidine in fibrillation. Quinidine slows the rate of passage of the impulse in the auricles, and, as the rate falls, the fibrillation waves become larger and more regular. In experimental flutter, when the flutter rate is high, the peaks become slightly irregular in time, and curves may be obtained which resemble those of fibrillation.

The importance of impure flutter lies in the fact that it shows that flutter and fibrillation are essentially similar, so that what has been proved in flutter (18) may reasonably be applied to fibrillation. The fact that flutter can be turned into fibrillation by the action of digitalis also points to a close relationship between the two.

Recently confirmation for this theory has come from electrical axes computed from the frontal, horizontal and sagittal planes (19). In flutter and fibrillation the path of the impulse lay more or less in a circle.

ACTION OF QUINIDINE ON CIRCUS MOVEMENT. The important feature of circus movement is the gap. If the gap closes, the circus movement must stop. If the gap increases, the wave may take another and a shorter course, if there is one open to it. The factors in circus movement that can be changed are the speed of conduction and the refractory period of the auricular muscle.

In heart muscle quinidine lengthens the refractory period and slows the rate of conduction. Transient bundle branch block has been produced when it was given to patients with sinus tachycardia (20). In addition it depresses the vagus, which has a different action upon the auricular muscle from that upon the conducting tissues, actually tending to improve conduction and shorten the refractory period. Quinidine, therefore, slows the circulating wave both by its direct action and by depressing the vagus, and the fibrillary rate may fall from the neighbourhood of 500 to below 250. With a slower auricular rate more impulses reach the ventricle: so during the administration of quinidine, before normal rhythm returns, the ventricular rate rises, unless digitalis has been given.

The action of quinidine upon the important gap is more variable, since it both increases the refractory period and slows conduction. Only if the refractory period is lengthened more than the speed of conduction is slowed, will the gap close, and the circus movement stop. This occurs in about 60 per cent of cases of auricular fibrillation.

ACTION OF DIGITALIS ON CIRCUS MOVEMENT. - Digitalis stimulates the vagus, and thereby increases the speed of the circulating wave, but it also has a direct action upon the auricular muscle which slows the speed of the wave. These effects oppose one another, and one or the other may predominate. In fibrillation the result is usually a quickening of the fibrillation rate, but sometimes the actions neutralise each other, and occasionally a slowing may occur.

In flutter the pace of the circulating wave will usually be quickened. If digitalis is pushed, the flutter wave may take a shorter path, and turn into fibrillation. If then digitalis is stopped, normal rhythm may return spontaneously.

Since in their important action digitalis and quinidine oppose each other, quinidine has been employed as a remedy for digitalis poisoning (21).

Auricular Fibrillation

Auricular fibrillation is a common disorder. It was present in 11 per cent of all electrocardiograms taken in a general hospital (22). It is found in the majority of cases of heart failure.

Ætiology. There are no histological lesions specific for fibrillation. Morbid changes are often present, but similar changes occur when the rhythm has remained normal. Of the predisposing causes cardiac rheumatism, *age*, and the influence of the vagus are important.

CARDI[illegible]

In mitral [illegible]
sooner or [illegible]
the patie[illegible] [illegible] series, including other valvular lesions, the incidence was greater *in those* who had previously had a prolonged P-R interval so that vagal influence may also be a factor (23), although it must be remembered that [illegible]

THE ELDERLY GROUP. Auricular fibrillation is found in elderly people who may show little other evidence of cardiac disease. The average age was higher in those patients who died with fibrillation, whether the underlying disease was hypertension, coronary disease and rheumatic heart disease (24).

VAGUS. Vagal influence is probably the underlying factor in a miscellaneous group including *electric shock*, *acute indigestion* or *appendicitis*, *ether anæsthesia*: also when fibrillation occurs in *digitalis poisoning* (25).

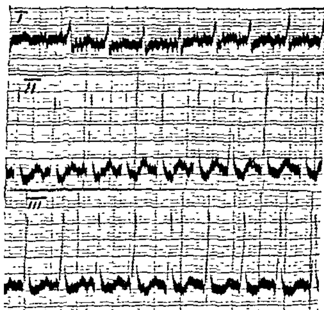


FIG 59

Auricular fibrillation Note rapid ventricular rate, 210, slight irregularity, alternation of R waves in lead II, and variation in T waves Tremor present from thyrotoxicosis, which is conducive to a very fast rate

HYPERTHYROIDISM. Auricular fibrillation is a well recognised complication of thyrotoxæmia, especially in the older patients (Fig. 59). The subject is discussed in Chapter VI.

OTHER CAUSES. Auricular fibrillation occurs as a rare complication, in *cardiac infarction* (p. 209), *pneumonia*, and in *cardiac syphilis*. It may follow *myocardial contusion* due to a non-penetrating injury of the chest (26) (p. 98). It is not uncommon after pulmonectomy for carcinoma of the lung (27). The only congenital

defect with which it occurs is a patent interauricular septum (p. 9).

Diagnosis. The diagnosis of auricular fibrillation is usually quite easy. The pulse is characteristic. It is totally irregular. The beats are irregular in strength and in spacing. There appears to be no relation between the size of any beat and that of the preceding pause: thus a small beat may follow a long interval, and a large beat succeed a short one. At no time can any succession of rhythmic beats be made out. There is a complete absence of a *dominant rhythm.*

EXAMINATION OF THE HEART. When the pulse rate is very fast, the irregularity may not be easy to appreciate. Auscultation at the apex may solve this difficulty, and the diagnosis should always be confirmed by auscultation. Some of the weaker contractions failing to overcome the aortic pressure, will cause no wave to be transmitted to the wrist. They may be heard at the heart, but will not be felt at the wrist. Sometimes these extra beats will make the irregularity more pronounced, though they will not always do so.

EFFECTS OF EXERCISE. The irregularity of fibrillation usually becomes more pronounced on moderate acceleration of the heart. When the rate is slow and there is any doubt as to the nature of the irregularity, the patient, if well enough, should be re-examined after *moderate* exercise, when the diagnosis will usually become

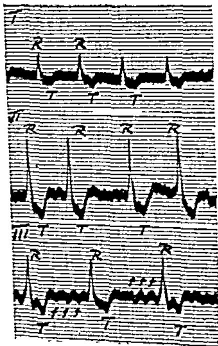


FIG. 60

Auricular fibrillation. Note fibrillary waves in lead III, inversion of T

THE ELDERLY GROUP. Auricular fibrillation is found in elderly people who may show little other evidence of cardiac disease. The average age was higher in those patients who died with fibrillation, whether the underlying disease was hypertension, coronary disease and rheumatic heart disease (24).

VAGUS. Vagal influence is probably the underlying factor in a miscellaneous group including *electric shock*, *acute indigestion* or *appendicitis*, *ether anæsthesia*: also when fibrillation occurs in *digitalis poisoning* (25).

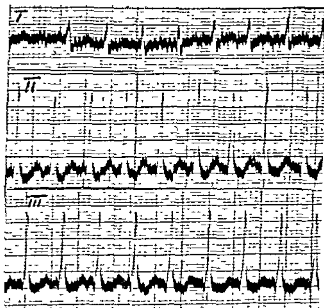


FIG 59

Auricular fibrillation Note rapid ventricular rate 210, slight irregularity alternation of R waves in lead II, and variation in T waves Tremor present from thyrotoxicosis, which is conducive to a very fast rate

HYPERTHYROIDISM. Auricular fibrillation is a well recognised complication of thyrotoxæmia, especially in the older patients (Fig. 59). The subject is discussed in Chapter VI.

OTHER CAUSES. Auricular fibrillation occurs as a rare complication, in *cardiac infarction* (p. 209), *pneumonia*, and in *cardiac syphilis*. It may follow *myocardial contusion* due to a non-penetrating injury of the chest (26) (p. 98). It is not uncommon after pulmonectomy for carcinoma of the lung (27). The only congenital

defect with which it occurs is a patent interauricular septum (p. 9).

Diagnosis. The diagnosis of auricular fibrillation is usually quite easy. The pulse is characteristic. It is totally irregular. The beats are irregular in strength and in spacing. There appears to be no relation between the size of any beat and that of the preceding pause · thus a small beat may follow a long interval, and a large beat succeed a short one. At no time can any succession of rhythmic beats be made out. There is a complete absence of a dominant rhythm.

EXAMINATION OF THE HEART. When the pulse rate is very fast, the irregularity may not be easy to appreciate. Auscultation at the apex may solve this difficulty, and the diagnosis should always be confirmed by auscultation. Some of the weaker contractions failing to overcome the aortic pressure, will cause no wave to be transmitted to the wrist. They may be heard at the heart, but will not be felt at the wrist. Sometimes these extra beats will make the irregularity more pronounced, though they will not always do so.

EFFECTS OF EXERCISE. The irregularity of fibrillation usually becomes more pronounced on moderate acceleration of the heart. When the rate is slow, and there is any doubt as to the nature of the irregularity, the patient if well enough, should be re-examined after moderate exercise, when the diagnosis will usually become

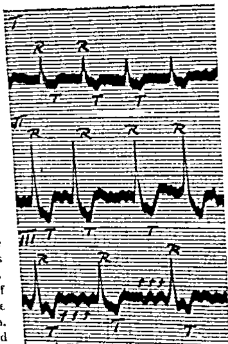


FIG 60

Auricular fibrillation Note fibrillary waves in lead III, inversion of T in all leads by digitalis

ELECTROCARDIOGRAMS. *Besides the total irregularity in the spacing of the ventricular complexes, the P (auricular) waves are absent. In place fibrillary waves are usually seen. They are rapid and irregular oscillations, occurring between 400 and 600 times a minute. They are often obvious at one part of a lead, and then die away a few beats later (see Fig. 60). They are always slightly irregular in shape and in time. They are much more prominent in some electrocardiograms than in others. The slower the fibrillary rate, the more obvious are the waves, as a rule. But they are always

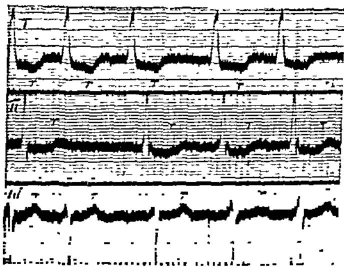


FIG. 61.

Auricular fibrillation Note irregularity, and absence of P waves The fibrillary waves are not conspicuous, but there are slight differences in the shape of the R-T phases, especially in lead III

present, and in the flat curves of fibrillation in which no oscillations may be visible between the ventricular complexes, they can still be seen superimposed upon the T waves, and careful inspection will show that no two T waves are exactly the same (Fig. 61).

Fibrillary waves are best seen in precordial leads to the right of the sternum. The largest deflections are obtained by means of an œsophageal electrode (28), but this is not without discomfort to the patient and is not applicable as a routine procedure.

DIFFICULTIES IN DIAGNOSIS. There are three conditions which are difficult to distinguish from fibrillation.

Multiple Premature Systoles, especially if they are arising from more than one focus in the heart, may give rise to an irregularity very similar to that of fibrillation. The exercise test may not assist as the rate is often already fast. A combination of fibrillation and premature systoles may cause difficulty; if the rate is slow, the fibrillation may be missed.

Partial Heart Block, with many dropped beats, when it occurs at a relatively rapid rate, may cause an arrhythmia clinically indistinguishable from fibrillation.

Auricular Flutter, when the ventricular rate is slow and irregular, may be impossible to distinguish from fibrillation without an electrocardiogram.

EFFECT OF THE ONSET OF FIBRILLATION. The effect of the onset of fibrillation depends upon the previous condition of the heart, and upon the speed at which the ventricles are driven.

The speed of the ventricles, varies inversely with that of the fibrillary waves. A healthy auriculo-ventricular bundle will not transmit impulses above a certain rate, and the higher the rate at which it is stimulated the fewer impulses will it conduct. If other conditions are equal, more stimuli will reach the ventricles with a fibrillary rate of 400 a minute than with a rate of 600. The highest recorded ventricular rate in fibrillation is 220, but it is not often that speeds of 160 are exceeded.

If conduction in the bundle is impaired, fewer stimuli will pass, and the onset of fibrillation may not cause any acceleration of the heart. Complete heart block with a slow and regular idioventricul[illegible]

rh

ha [illegible] people the ventricular rate may be but little affected by the fibrillation because of latent heart block, and they may be unable to remember when the arrhythmia began.

COURSE. Auricular fibrillation lowers the efficiency of the heart. The lowered efficiency is due in part to the irregularity, since the level of the systolic blood pressure and the pulse pressure are directly related to the preceding cycle length (29). When the ventricular rate is rapid, many beats are ineffective and do not reach the pulse. Under digitalis therapy the maximum efficiency is attained when the apex and pulse rates are most nearly the same.

ELECTROCARDIOGRAMS. Besides the total irregularity in the spacing of the ventricular complexes, the P (auricular) waves are absent. In place fibrillary waves are usually seen. They are rapid and irregular oscillations, occurring between 400 and 600 times a minute. They are often obvious at one part of a lead, and then die away a few beats later (see Fig. 60). They are always slightly *irregular in shape and in time.* They are much more prominent in some electrocardiograms than in others. The slower the fibrillary rate, the more obvious are the waves, as a rule. But they are always

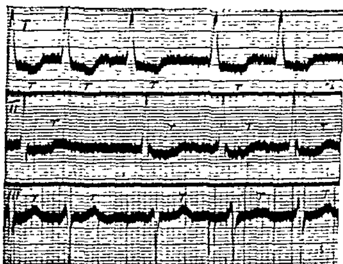


FIG. 61

Auricular fibrillation Note irregularity, and absence of P waves The fibrillary waves are not conspicuous, but *there are slight differences in the shape of the R-T phases,* especially in lead III

present, and in the flat curves of fibrillation in which no oscillations may be visible between the ventricular complexes, they can still be seen superimposed upon the T waves, and careful inspection will show that *no two T waves are exactly the same (Fig. 61).*

Fibrillary waves are best seen in precordial leads to the right of the sternum. The largest deflections are obtained by means of an œsophageal electrode (28), but this is not without discomfort to the patient and is not applicable as a routine procedure.

DIFFICULTIES IN DIAGNOSIS. There are three conditions which are difficult to distinguish from fibrillation.

occur in chronic rheumatic heart disease and in hyperthyroidism; occasionally it is seen in acute rheumatic carditis. Paroxysms may follow cardiac infarction or an acute infection, such as influenza. It may be associated with patent interauricular septum. Cases have been recorded after pulmonectomy (27).

Diagnosis. Auricular flutter is due to a continuous regular wave circulating in the auricles at an average frequency of 300 revolutions a minute. This wave sends down impulses to the ventricles which usually answer half of them (1 : 2 response). The ventricles will then beat at a regular rate of about 150. In some patients the ventricular response is slower (1 : 3 or 1 : 4 response); the rate is then less than 150, and the rhythm is *irregular*, except in rare cases where complete heart block co-exists.

Physical Examination. If a patient has a regular pulse of about 130 to 170 which remains constant in all positions, whether he is up or at rest, the tachycardia is likely to be due to auricular flutter. The jugular pulse in the neck should be examined closely. The rapid and regular auricular rhythm can sometimes be observed in the pulsation of the jugular veins when the patient lies flat; and it may be possible on occasions to make out waves which are much faster than the ventricular rate, especially if pressure on the carotid sinus is effective. Occasionally in these patients the flutter sounds can be heard (32), and the auricular movements may cause a perceptible vibration of the chest wall. The contractions of the auricle can occasionally be seen on the screen with the patient in the right oblique position and barium in the œsophagus; the column of barium vibrates.

Carotid sinus pressure may cause the ventricular rate to become slow and irregular for as long as the pressure is maintained; then the original rapid rate is resumed. The flutter waves of the external jugular veins may be seen to persist. This serves to distinguish flutter from other forms of paroxysmal tachycardia, but occasionally a sinus tachycardia responds in a similar manner. If the pulse is from 100 to 120 and irregular, mild exercise may cause it to accelerate to about 150, and to become regular.

Too much reliance must not be placed on these methods of diagnosis. By their means flutter may occasionally be diagnosed positively, more often it can be inferred by exclusion. In most cases an electrocardiogram is required.

The point at which this occurs varies in different individuals, but it will not usually be reached until both rates are under eighty.

Exercise causes an undue acceleration of the heart in fibrillation. There is also a delay in the return to the resting level. The *acceleration is usually* due to a decrease in the vagal tone. The fibrillation waves become slower, and so a greater number of stimuli pass down the bundle. The effect can be reproduced by an intravenous injection of atropine (30). The acceleration can be controlled to some extent by digitalis, but larger doses are required than suffice to control the rate at rest.

Emotion can lead to acceleration through an increase in the conductivity of the bundle due to over-action of the sympathetic. This occurs also in fever. In nervous subjects with a tendency to sympathetic over-activity the response is exaggerated. This tendency is particularly noticeable in hyperthyroidism. In these cases sedatives should be given as well as digitalis. Elderly people, who often have a predominant vagal influence, and more placid types, can manage with much less digitalis.

Prognosis. Auricular fibrillation occurs so commonly as a terminal condition, or in hearts which are damaged already with the effects of a rheumatic infection, that the gravity of the prognosis is apt to be exaggerated The condition itself occasions a measure of cardiac disability, but the prognosis as regards life depends upon the state of the ventricular muscle. The longest recorded case of persistent fibrillation, according to Lewis, is thirty-two years. Such a case now would probably be restored to normal rhythm with quinidine. Even with mitral stenosis fibrillation has persisted up to twenty years (31). These cases are exceptional, however, and auricular fibrillation must be regarded as a serious incubus upon the heart. When it occurs in a heart which is already meeting the demands upon it with difficulty, failure may come on rapidly.

Auricular Flutter

Auricular Flutter is an uncommon disorder, occurring in many types of heart disease. The average age of onset is somewhat later than in fibrillation, most patients being from forty to seventy, although examples have been found in infancy. Flutter may

there is any disease of the conducting tissue, since most normal hearts would probably respond in that way. It is merely a method of expressing the ratio of the auricular to the ventricular rates.

When the ventricular complexes are abnormal as in bundle branch block and recent infarction the flutter peaks may be obscured (33). In other cases, too, the flutter peaks may not be obvious and the curves may resemble auricular paroxysmal tachycardia. It is only in 1-2 flutter that difficulties arise, and increasing the block by means of carotid sinus pressure, or with digitalis, will enable the diagnosis to be made (Fig. 63).



Fig. 63.

Auricular flutter. Pressure carotid sinus (X) causes transient *ventricular* standstill. Ventricular escape (V E) occurs

1-1 Flutter. The human ventricle is not *capable* of maintaining rates of over 300, and speeds of over 200 are not well tolerated. The lower flutter rates are among those which can just be maintained, so that every impulse may be transmitted and the ventricle will then beat at a speed of 200 or *more*. Attacks have been *recorded* in which the ventricular rate was *between* 250 and 300, and several in which it was about 200, mostly *occurring during* the auricular slowing brought about by *quinidine* (34). These attacks are provoked by *exertion*. They are usually *serious*, and sometimes cause loss of consciousness, and they may account for some of the deaths which *are* classified as syncope (Fig. 65A and B).

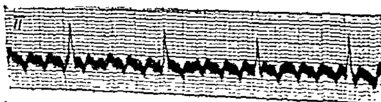


Fig. 64

Auricular flutter. Auricular *rate* 360, ventricular *rate* 75. Ratio about

Electrocardiograms. The electrocardiograms of flutter are usually distinctive. Besides the ventricular deflections, oscillations of the fibre are seen which have a sharp uprising and a more gradual fall. They are seen better in leads II and III than in lead I, and are most prominent in precordial leads taken to the *right of the sternum*. These oscillations are called the "flutter peaks," and it is noticeable that as soon as one ends the other begins. They are perfectly constant in shape and in time in each subject, and they have a very similar shape in different subjects, although the rate may vary considerably. The usual rate is about 300, but they have been found as low as 180 and as high as 360 a minute (Fig. 62).

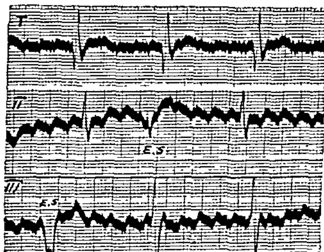


FIG 62

Auricular flutter Auricular rate 250 As usual, the *flutter oscillations appear only in two leads* The ventr [illegible] heart block [illegible]

1-2 FLUTTER. Usually every other stimulus is transmitted to the ventricles so that the ventricular rate is regular, and varies from 130 to 180. Sometimes a stimulus will be dropped at intervals so that at one moment every other impulse *and at another every* third will be transmitted. The ventricular rate will then be about 120 and slightly irregular. *When every other stimulus* is answered, 1-2 heart block is said to be present. *This does not imply* that

Course and Prognosis. The onset of continuous flutter is a more serious event than the onset of fibrillation (34). Ambulant cases of flutter are not so easily controlled by digitalis, and they are liable to an abrupt doubling of the ventricular rate on exertion. A change from flutter to fibrillation is almost always beneficial to the patient.

As in fibrillation the prognosis as to life depends upon the underlying cardiac condition. One case had continuous flutter for twenty-four years with unimpaired efficiency of the heart (35).

Paroxysmal Tachycardia

A paroxysm of tachycardia is a bout of rapid heart action which starts quite suddenly, has a variable duration, and ends as suddenly as it began. The rate of the ventricles varies from 120 to 300 a minute. Some patients are prostrated by the attack and have to lie down till it is over; others are but little inconvenienced. The patients complain of palpitation and perhaps suffocation with a sense of fluttering in the chest. The rapid beating of the heart is often distressing. Precordial pain may develop. The blood pressure falls and giddiness and faintness may be caused by the defective cerebral circulation. There may be acute mental disturbances such as hallucinations, and epileptiform convulsions may occur. Nausea is sometimes noted.

The duration of a paroxysm is very variable. It may only consist of a few beats, or last for days. Most paroxysms end within two days, but some have lasted for a year or more.

In prolonged paroxysms the circulation is slowed and the heart may fail. This is more likely to occur if the heart was previously diseased. The patient becomes orthopnœic, and may vomit: or precordial pain may be felt. Venous engorgement and cyanosis appear. there may be congestion of the lungs. The attacks, though alarming, rarely end fatally, and the patient rapidly recovers from the heart failure when normal rhythm returns.

Paroxysms of tachycardia may be due to transient auricular fibrillation or flutter, to auricular paroxysmal tachycardia, or to ventricular tachycardia. Ventricular fibrillation is so closely associated with the last that it is also considered here.

Paroxysmal Auricular Fibrillation Paroxysms of fibrillation usually end spontaneously within [illegible]

SLOW VENTRICULAR RATE IN FLUTTER. When the ventricle responds sometimes to every third, and sometimes to every fourth impulse, the rhythm will be irregular, and the rate will be comparatively slow. When the rate is below 120 it is probable that *the bundle is diseased, although the expressions 1-3 and 1-4 heart* block are again merely methods of expressing a ratio (Fig. 64). When the rate is under 60, disease of the conducting tissue is certainly present, and complete heart block is sometimes met with in flutter (Fig. 62).

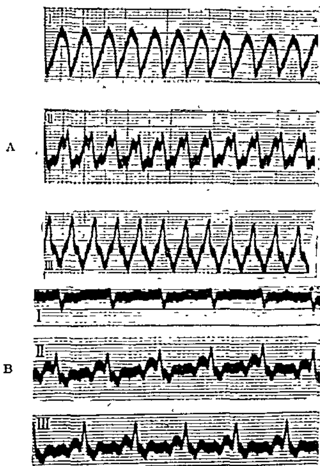


FIG 65

A —Auricular flutter, nearly 300 1-1 ventricular response

B —Auricular flutter 1-2 ventricular response From the same case as A

Course and Prognosis. The onset of continuous flutter is a more serious event than the onset of fibrillation (34). Ambulant cases of flutter are not so easily controlled by digitalis, and they are liable to an abrupt doubling of the ventricular rate on exertion. A change from flutter to fibrillation is almost always beneficial to the patient.

As in fibrillation the prognosis as to life depends upon the underlying cardiac condition. One case had continuous flutter for twenty-four years with unimpaired efficiency of the heart (35).

Paroxysmal Tachycardia

A paroxysm of tachycardia is a bout of rapid heart action which starts quite suddenly, has a variable duration, and ends as suddenly as it began. The rate of the ventricles varies from 120 to 300 a minute. Some patients are prostrated by the attack and have to lie down till it is over; others are but little inconvenienced. The patients complain of palpitation and perhaps suffocation with a sense of fluttering in the chest. The rapid beating of the heart is often distressing. Precordial pain may develop. The blood pressure falls and giddiness and faintness may be caused by the defective cerebral circulation. There may be acute mental disturbances such as hallucinations, and epileptiform convulsions may occur. Nausea is sometimes noted.

The duration of a paroxysm is very variable. It may only consist of a few beats, or last for days. Most paroxysms end within two days, but some have lasted for a year or more.

In prolonged paroxysms the circulation is slowed and the heart may fail. This is more likely to occur if the heart was previously diseased. The patient becomes orthopnœic, and may vomit; or precordial pain may be felt. Venous engorgement and cyanosis appear: there may be congestion of the lungs. The attacks, though alarming, rarely end fatally, and the patient rapidly recovers from the heart failure when normal rhythm returns.

Paroxysms of tachycardia may be due to transient auricular fibrillation or flutter, to auricular paroxysmal tachycardia, or to ventricular tachycardia. Ventricular fibrillation is so closely associated with the last that it is also considered here.

Paroxysmal Auricular Fibrillation. Paroxysms of fibrilla-

is not likely to return after a week, although it has done so spontaneously after two years (36).

Paroxysms occur under three conditions. A series of paroxysms may precede the onset of permanent fibrillation. This is not uncommon in mitral stenosis or hyperthyroidism. It seems as though the auricular muscle has reached a state when any stimulus will be sufficient to excite fibrillation. *Auricular premature* systoles are often present at this stage. The paroxysms may last from a few beats to some hours.

In another group are the isolated paroxysms. They have usually a definite exciting cause, such as a coronary occlusion, or they arise during the course of an infection. In the same category are the attacks due to vagal influence, such as those caused by electric *shock, or following some mental disturbances; or caused by direct* stimulation of the vagus by mecholyl (37).

In true paroxysmal fibrillation the patient may undergo a succession of these attacks at shorter or longer intervals over a number of years. Often a careful search fails to find any satisfactory cause. In some cases toxic conditions, such as cystitis or pyelitis, are associated with the paroxysms. The attacks are not *dangerous, but they may give rise to much disability.* Sometimes they end by the fibrillation becoming established; sometimes the condition proves amenable to treatment.

Paroxysmal Auricular Flutter. One quarter of all cases auricular flutter are purely paroxysmal, and attacks are often associated with paroxysms of fibrillation (34). Paroxysms of flutter tend to recur and become more frequent, and they easily *lead to heart failure if at all prolonged.*

Cases with numerous short attacks consisting of a few flutter peaks only are sometimes found. Single flutter peaks may occur in such records (38) (Fig. 66).



Fig 66

The arrow marks the end of a paroxysm of flutter The next attack starts with an auricular extra-systole (E S)

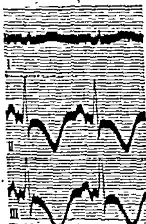


Fig 67
Negative T waves after a long paroxysm of auricular tachycardia

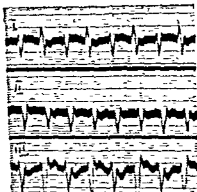


Fig 68
Nodal tachycardia at a rate of 194 with bidirectional ventricular responses (QRS, 0 09 sec)

Auricular Tachycardia. In auricular tachycardia the heart beats at a rate varying from 120 to 300, but in most cases the rate is about 180. As a rule the rhythm is remarkably regular, the beats being evenly spaced to a fraction of a second. Sometimes the rhythm is interrupted by ventricular premature systoles. The rate is not usually influenced by posture or by emotion. Pressure on the carotid sinus will not alter the rate, although it may terminate the attack. The mechanism is not under the control of the central nervous system. Pulsus alternans may appear during the attack

The ventricular complexes are usually of the normal supraventricular type. Sometimes, however, the ventricular complexes shows aberration during the attack (Fig. 68) and the curves will then simulate a paroxysm of ventricular tachycardia. In most attacks, unless the beginning or end has been recorded, the P waves cannot be seen, being buried in the QRS or T waves. When present they are abnormal and usually inverted (Fig. 69). In the comparatively rare type of nodal tachycardia inverted P waves follow the QRS ...
for
(Fig

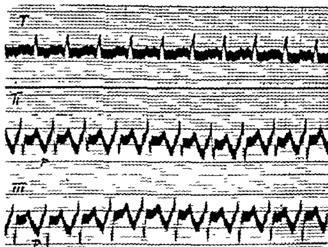


Fig. 69

Auricular tachycardia. Rate 180. Note inverted P waves.

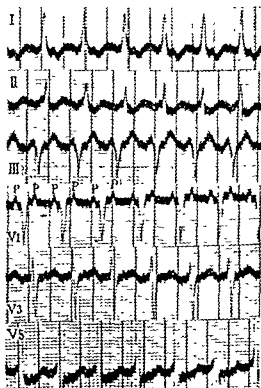


Fig. 70

Auricular tachycardia with 2:1 heart block. Auricular rate is 320. Ventricular rate is 160.

Auricular tachycardia may be associated with A-V heart block (40) (Fig. 70). The attacks last longer than in the common type and cause more disability. One patient without heart disease died after three months continuous tachycardia. Tachycardia may only be noticed by the patients when a 1-1 response is present. Treatment on the whole is ineffective though digitalis increases the block, and quinidine may restore normal rhythm. 2-1 auriculoventricular block or a reversed Wenckebach phenomenon may occur. Complete dissociation has been recorded (41). In one series of forty cases digitalis seems to have been a factor (42). Nearly all had had congestive failure before the auricular tachycardia began and had received digitalis, frequently to excess. Half of these patients died.

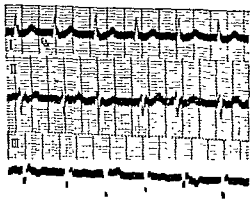
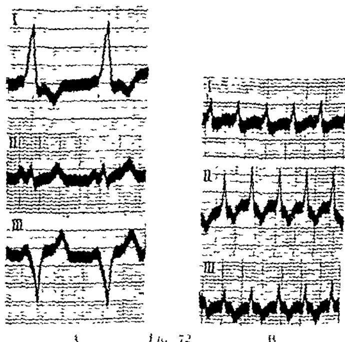


FIG 71
Auricular tachycardia at 120 with alternating cycle lengths

There is a close relationship between this type of auricular tachycardia and paroxysmal auricular fibrillation and flutter. Of 14 cases of auricular tachycardia, who had also paroxysms of fibrillation and flutter, all but one had 2-1 block (43). Alternation of the cycle length of the complexes occurs at times (44) (Fig 71). Digitalis and quinidine may both slow the auricular rate or stop a paroxysm On account of these *facts it* has been suggested that auricular tachycardia may be due to a circus movement involving the S A node when the P waves are upright, and the A.V. node when the P waves are inverted (45). Digitalis would slow the

circus through its action on the nodal tissue quinidine by acting directly *on the auricular muscle*. The slow speed of the circus as well as the iso-electric periods separating the P waves, compared with the continuous activity of the fibres in *auricular flutter or fibrillation*, could be accounted for by the slow rate of conduction in either node. An alternative suggestion is that the average auricular rate in auricular tachycardia is faster than in flutter and that a 2-1 A-V block is the rule, alternate P waves being buried



A   Fig. 72   B

A Wolff-Parkinson White syndrome

B —Paroxysm of auricular tachycardia from the same case

in the QRS (46). However, when the electrical axes were calculated for auricular tachycardia, the impulse, *in contradistinction to the findings in flutter, seemed to pursue a normal course* (19)

In exceptional cases the *usual rules for paroxysmal tachycardia* do not apply. Thus two girls had auricular *tachycardia*, for six years and two years respectively at a rate of 180 when standing, and 150 when sitting, while normal rhythm at 90 often returned when lying, 2-1 heart block being present at other times (47). It is possible that this *orthostatic tachycardia* may account for

paroxysms of very long duration, as in a man who had auricular tachycardia for forty-three years without much disability, broken only for a period of four weeks following cardiac infarction (48). A focus near the S A. node may have been responsible for another attack which ended gradually after seventy days, since the tachycardia increased with emotion and diminished during sleep (49). There is an association between auricular tachycardia and the Wolff-Parkinson-White syndrome. When the accessory bundle is present, attacks are common. During the attack the ventricular complexes may be more normal (Fig. 72A and B)

Paroxysms may occur in infancy with rates varying from 250 to 300 (50) The child is restless, then apathetic, and the pulse often imperceptible (51) Vomiting and cyanosis may occur. Fever and leucocytosis are present. Congestive failure may follow.

Prognosis. If there is no associated heart disease, the expectation of life in auricular tachycardia does not differ from the normal. In 750 cases attacks had been present on the average for 25 years, and the longest history was sixty-four years (52). It is impossible to predict the number of attacks any patient is likely to have. The attacks may cease spontaneously, or the patient may re-act to treatment; but others continue unchecked Occasionally the attacks become more frequent and last longer, with more serious and sometimes fatal effects (52)

Ventricular Tachycardia

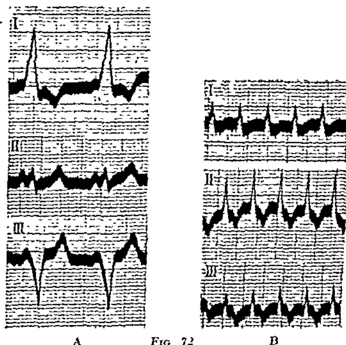
D...

ec

as ... premature systoles (Fig. 73). They must ...

... branch block. To do so certain criteria ha[ve] been established. Of these, the most reliable is the demonstrati[on] of an independent auricular rhythm with P waves occurring [at] a slower rate (Fig. 74). The lead from the third right interspac[e is] useful for this purpose (53). Other acceptable criteria are [the] presence of ventricular premature systoles before and after [the] paroxysm, similar in shape to the complexes of the paroxysm; [the] onset of the paroxysm with an abnormal ventricular complex ...

circus through its action on the nodal tissue: quinidine by acting directly on the auricular muscle. The slow speed of the circus as well as the iso-electric periods separating the P waves, compared with the continuous activity of the fibres in auricular flutter or fibrillation, could be accounted for by the slow rate of conduction in either node. An alternative suggestion is that the average auricular rate in auricular tachycardia is faster than in flutter and that a 2-1 A-V block is the rule, alternate P waves being buried



A FIG 72 B

A —Wolff-Parkinson-White syndrome

B —Paroxysm of auricular tachycardia from the same case

in the QRS (46). However, when the electrical axes were calculated for auricular tachycardia, *the impulse, in contradistinction* to the findings in flutter, seemed to pursue a normal course (19).

In exceptional cases the usual rules for paroxysmal tachycardia *do not apply.* Thus two girls had auricular tachycardia, for six years and two years respectively, at a rate of 180 when standing, and 150 when sitting, while normal rhythm at 90 often returned when lying, 2-1 heart block being present at other times (47). It is possible that this *orthostatic tachycardia* may account for

paroxysms of very long duration, as in a man who had auricular tachycardia for forty-three years without much disability, broken only for a period of four weeks following cardiac infarction (48). A focus near the S.A. node may have been responsible for another attack which ended gradually after seventy days, since the tachycardia increased with emotion and diminished during sleep (49). There is an association between auricular tachycardia and the Wolff-Parkinson-White syndrome. When the accessory bundle is present, attacks are common. During the attack the ventricular complexes may be more normal (Fig. 72A and B).

Paroxysms may occur in infancy with rates varying from 250 to 300 (50). The child is restless, then apathetic, and the pulse often imperceptible (51). Vomiting and cyanosis may occur. Fever and leucocytosis are present. Congestive failure may follow.

Prognosis. If there is no associated heart disease, the expectation of life in auricular tachycardia does not differ from the normal. In 750 cases attacks had been present on the average for 25 years, and the longest history was sixty-four years (52). It is impossible to predict the number of attacks any patient is likely to have. The attacks may cease spontaneously, or the patient may re-act to treatment; but others continue unchecked. Occasionally the attacks become more frequent and last longer, with more serious and sometimes fatal effects (52).

Ventricular Tachycardia

[illegible]
ec [illegible]
as [illegible] premature systoles (Fig. 73) They must [illegible]

[illegible] branch block. To do so certain criteria have been established. Of these, the most reliable is the demonstration of an independent auricular rhythm with P waves occurring at a slower rate (Fig. 74). The lead from the third right interspace is useful for this purpose (53) Other acceptable criteria are the presence of ventricular premature systoles before and after the paroxysm, similar in shape to the complexes of the paroxysm; the onset of the paroxysm with an abnormal ventricular complex; and

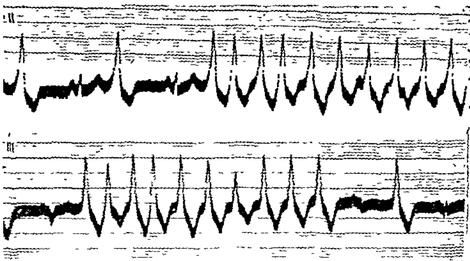


Fig. 73
Paroxysmal ventricular tachycardia and extrasystoles from the same focus

ventricular complexes occurring regularly and rapidly in auricular fibrillation (54). Rarely there may be retrograde conduction with partial block. Inverted P waves will then follow most of the ventricular complexes, but some impulses will be blocked and so the P waves will be absent.

The ventricular rate during an attack varies from 100 to 300. The rhythm is usually regular, but sometimes there are slight

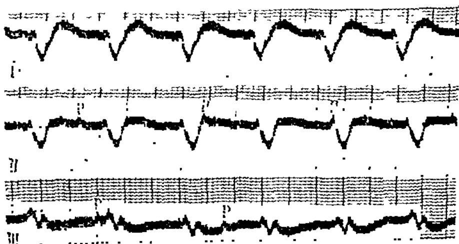


Fig. 74
Ventricular tachycardia at 110. Auricular rate at 65.

variations in speed which may be perceptible clinically. The sounds of the heart may vary in intensity. Carotid sinus pressure has no effect upon the tachycardia. Attacks may last from a few beats to two months (55). Long attacks usually end fatally; those after coronary occlusion are particularly dangerous.

Ætiology. Ventricular tachycardia is much less common than auricular tachycardia, and it is usually associated with severe myocardial disease. Attacks have been recorded in children (56). Only in one-fifth of the cases is the heart otherwise normal. In the remainder either cardiac infarction, or digitalis overdosage or disease of the conducting tissues, auriculo-ventricular or bundle branch block, is present (54). After cardiac infarction digitalis is usually withheld owing to the risk of ventricular tachycardia, but of six cases occurring after infarction digitalis had *only been given* in two (53). In A-V heart block ventricular tachycardia *often* precedes ventricular fibrillation which is one of the causes of Stokes-Adams attacks (see p. 238).

Theories of Causation. The *Re-entry Theory* has been applied to ventricular tachycardia as well as to ventricular premature systoles on the following grounds. In all the three associated myocardial lesions conduction is impaired; since digitalis causes heart block, and an infarcted area does not conduct normally. A normal ventricular premature systole spreads rapidly, and all the ventricular muscle is refractory at the same time. If conduction is defective, the spread might be uneven, owing to the increased refractoriness of some areas, and re-entry might occur. Ventricular tachycardia by this theory is due to *circus movement*, and is closely linked to ventricular fibrillation.

Supernormal Phase. Some cases cannot be explained satisfactorily by a theory of circus movement. In one instance a ventricular tachycardia was interrupted at times by an auricular tachycardia at a higher rate, and the transition was gradual (57). This suggests strongly one ectopic focus being superseded by another. In such cases it seems likely that a repetitive discharge of stimuli from an ectopic focus during the supernormal phase causes the paroxysm (54). It is even possible that the focus may be in the node or the bundle, and that the form of the ventricular complexes may be due to aberration owing to their prematurity. Probably some such mechanism accounts for paroxysms when the

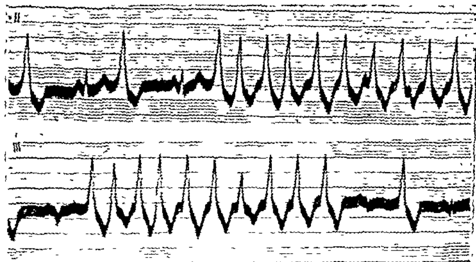


Fig. 73
Paroxysmal ventricular tachycardia and extrasystoles from the same focus

ventricular complexes occurring regularly and rapidly in auricular fibrillation (54). Rarely there may be retrograde conduction with partial block. *Inverted P waves will then follow most of the ventricular complexes, but some impulses will be blocked and so the P waves will be absent.*

The ventricular rate during an attack varies from 100 to 300. The rhythm is usually regular, but sometimes there are slight

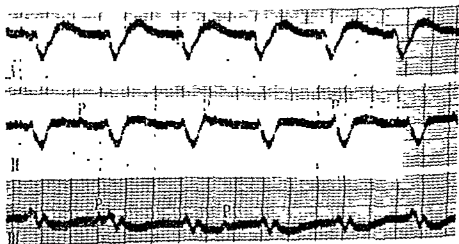


Fig. 74
Ventricular tachycardia at 110. Auricular rate at 65

acceleration to 120, or else there may be short runs of ventricular tachycardia. Ventricular premature systoles from a constant focus invariably precede fibrillation, the onset of which seems to be facilitated by the gradual acceleration.

During the initial fibrillary period which also may last from some minutes to days, short bursts of ventricular fibrillation are seen in which the size of the complexes is diminished.



Fig 75
Bidirectional ventricular tachycardia

The fully developed attack of ventricular fibrillation lasts up to six minutes Inco-ordinate contractions occur with a frequency of 240 to 260 (Fig. 44). The oscillations *in the* electrocardiogram vary also in amplitude, and they may change *abruptly* to regular and equal complexes at a rate of 130 to 170, and then revert to inco-ordination With asphyxia the rate may fall to 90 and the oscillations may be *only* 2 mms. in amplitude.

After the *attack* there is a post-undulatory pause or cardiac standstill which may last up to a minute (60). The auricles cease beating after about ten seconds Some time after recovery paroxysms of auricular fibrillation or flutter may occur.

Attacks of ventricular fibrillation have been precipitated by injections of adrenalin given for Stokes-Adams disease, assumed to be due to ventricular *standstill. The* arrhythmia has usually been recorded in dying hearts, but some patients have had numerous attacks over a period of years (59)

fifty grains can be dissolved in 5 per cent glucose saline and given intravenously by drip infusion at the rate of 100 c.c. an hour (65). Quinidine bi-hydrochloride is soluble in 1-1 and gr. iii can be made up in a 2 c.c. ampoule. This is the most used preparation for intravenous administration, and 10 grains or more can be given at a time if necessary. The bi-hydrochloride of quinine, which is soluble in 1 in 0.6, is not so effective as quinidine but can be given intramuscularly. Quinine is irritating to the tissues, but 10 grains can be injected two-hourly utilizing different sites for each injection.

For most cases of auricular fibrillation the drug can be given satisfactorily by mouth. The following scheme is safe and effective, though many other methods have been used.

Thirty grains are given, divided into six doses at two-hourly intervals. The apex rate is charted hourly to note if normal rhythm returns, or if undue acceleration occurs. In either case quinidine is stopped. The pulse is often found to have become regular when the patient wakes next morning. If it has not done so, the same quantity of quinidine is repeated on the second day, and again on the third. If the case is still refractory, digitalis is substituted until the apex rate has been brought down to below 80. It is then stopped and quinidine repeated for another two or three days. If after the third course of three days the fibrillation persists, the attempt to restore normal rhythm is given up, but more than two-thirds of all cases will respond at some time during the course.

After the restoration of normal rhythm it is usually advisable for the patient to remain in bed a further week to avoid relapse. Unless the cause of the fibrillation has been eliminated, as in post-operative thyrotoxic cases, 10 to 15 gr. of quinidine should be given daily as a holding dose, and should be continued until the patient is again living his ordinary life.

Sometimes it may be advisable to give 35 gr. during the second and third courses. Larger doses than this have been given, but they are not satisfactory. They may cause severe headache, and patients who require them are likely to relapse. Another and slower method is to give 5 gr. the first day, 10 the second, and so increase the daily dose gradually until a maximum of 30 gr. daily has been reached. This dose is continued for two or three ...

Ventricular fibrillation may supervene in many experimental procedures upon the heart. Attacks can be induced by a single strong shock during the supernormal phase in late systole. It is suggested that the re-entering wave involves progressively smaller blocks of heart muscle and that the divided waves have a shorter circus (61). To combat this a few weaker shocks have been applied at intervals of about a second. This was found to cause a progressively coarser type of fibrillation until the process was arrested. This method was successful in stopping fibrillation in a large number of experiments on dogs.

Treatment

Auricular Fibrillation. The treatment of auricular fibrillation may aim at controlling the rate and thereby increasing the strength of the ventricular contraction. This is effected by means of digitalis (see p. 347). Normal rhythm may return after digitalis therapy, especially if congestive failure has been present, but this follows the general improvement in the circulation and is not due to any specific effect upon the auricles

Quinidine *is given to selected patients with auricular fibrillation in order to restore normal rhythm*

Quinidine is a general cardiac depressant and causes both pulse rate and blood pressure to fall. In patients with physiological tachycardia it may produce bundle branch block, and the abnormal ventricular deflections found during quinidine administration are probably due to depression of conduction in the ventricles.

Toxic Effects. Tinnitus and headache are common with large doses. Vomiting and diarrhœa sometimes occur. A febrile reaction with leucopenia has also been recorded (62).

Commercial quinidine contains 80 per cent pure quinidine and 20 per cent hydroquinidine. Pure quinidine is twice as toxic as the commercial product since hydroquinidine is not toxic and therapeutically inert (63). Elimination is rapid, 95 per cent leaving the blood in a few minutes of an intravenous injection (64). By mouth the maximum effect is obtained in about two hours.

Methods of Administration. Quinidine can be given orally as quinidine sulphate. Tablets containing gr. v or 0.2 gm. (gr. iii) or 0.3 gm. (gr. vi) are available. Quinidine sulphate is only soluble in 1-90 parts of water, but by vigorous shaking

increases with advancing age (66). Quinidine is seldom given to patients with mitral stenosis, since fibrillation will always be liable to recur, and, when the ventricular rate is uncontrolled with digitalis, this may lead to congestive failure.

TREATMENT OF PAROXYSMAL FIBRILLATION. Intravenous quinidine bi-hydrochloride (gr. iii) may stop the paroxysm at once. If this is not available, the patient should be given a sedative such as omnopon, gr. 1/3, and five or six grains of quinidine sulphate. The quinidine should be repeated very two hours till the attack is over.

To prevent paroxysms quinidine sulphate is often effective in doses of 15 to 20 grains daily. Larger doses, up to 70 grains, daily, have been given, but they tend to cause A-V heart block and bundle branch block (67) Moderate doses of digitalis are sometimes effective as prophylactic. The number of paroxysms over fifteen months was reduced to one-tenth by the intravenous injection, during the paroxysm, of cedilanid, a glycoside derived from digitalis lanata, followed by 0.5 to 1 mg. by mouth daily (68). Some aim at inducing permanent fibrillation by full doses of digitalis.

TREATMENT OF AURICULAR FLUTTER. *Digitalis.* This is the most satisfactory method As the ventricular rate slows under the drug the rhythm will become *irregular*, although occasionally it may pass straight to a 1 . 4 *rhythm.* When it has come down to below 80 a careful watch is kept In about 30 per cent of cases the rhythm will become completely irregular, since the flutter will have turned into *fibrillation.* If digitalis is now stopped, normal rhythm may return spontaneously. If *it does* not, quinidine may be tried Digitalis may have to be pushed to a full or even toxic dose

Quinidine is sometimes effective in removing flutter, but it is seldom used. As in fibrillation, quinidine slows the auricular rate, and when it has fallen to 200 a minute, or less, the ventricles may answer every stimulus. This 1 : 1 response is a reaction to be avoided Quinidine should be reserved for those cases who have not responded to a thorough course of digitalis.

1 : 1 *Flutter.* Carotid sinus pressure should be used to change the response quickly to a slower rate but this effect may only be transient (see Fig 63) Since these attacks are related to exertion

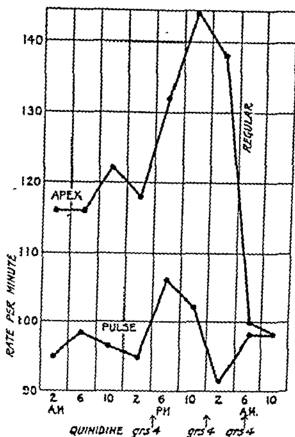


Fig 76
Showing the effect of quinidine on the heart rate and rhythm in fibrillation

unless the rhythm becomes normal. Some prefer to give a preliminary course of digitalis in order to avoid the ventricular acceleration due to the slowing of the circulatory wave

Selection of Cases. Quinidine should always be given to patients with otherwise normal hearts who develop fibrillation. It is also most useful in thyrotoxic cases in whom normal rhythm has not returned spontaneously after thyroidectomy or after a course of thiouracil. Almost all these cases will respond.

Congestive failure, active infections, and gross cardiac enlargement are generally regarded as contra-indicating quinidine. In old-standing cases of fibrillation clots may be dislodged from the auricle and give rise to emboli, and the risk of auricular thrombi



FIG. 77.

The arrow indicates pressure on the carotid sinus. The heart rate slows, and the P waves disappear. Sinus rhythm is replaced by nodal rhythm temporarily.

(Fig. 77). Or there may be standstill of the whole heart (see p. 230).

Technique of Compression. The patient may be sitting or lying. If lying, the head should be slightly extended and the face turned a little to the opposite side. The ampullary dilatation of the carotid should be located just short of the point at which the vessel disappears under the angle of the jaw. The sinus should then be pressed firmly, or massaged up and down by the palmar surface of the thumb if the patient is lying; if he is sitting, the operator stands beyond him and uses his fingers (71). One side should be pressed at a time, the right side first. The pressure is maintained for about half a minute, unless the heart rate reacts. Both sides may be tried at once, if either fails alone.

Carotid sinus pressure may terminate an attack of auricular tachycardia. In auricular flutter, the ventricular rate is slowed during the time that the pressure is maintained; on release of pressure the original rate returns (Fig. 63). This serves to distinguish doubtful cases. Carotid sinus pressure has no effect upon ventricular tachycardia. The pressure may cause abrupt slowing in normal sinus tachycardia.

Vagal Stimulation can also be brought about by ipecac. One or two drachms of the syrup can be given and repeated in forty-five minutes, if the patient has not vomited or the attack has not stopped (72). Treatment is quite safe though somewhat unpleasant. Mecholyl (acetyl B methyl choline chloride) in doses of 5-10 mg. given subcutaneously stimulates the vagus directly. It is sometimes efficacious in auricular tachycardia, but undesirable reactions are apt to occur. Thus one child lost consciousness after 10 mg., the pulse falling to 30 (73) and in another after 8 mg. the pulse fell to 20 with concomitant ...

hydrochloride, gr. x, should be given slowly by intravenous injection, preferably under electrocardiographic control. By so doing the injection can be stopped if normal rhythm is observed to return. In long attacks in which the patient seems likely to die, the following procedures have proved successful. Quinidine sulphate, gr. iii, given every hour, slowed the rate and relieved the symptoms in one case, although it did not restore normal rhythm. Intramuscular injections of quinine bi-hydrochloride restored normal rhythm after 240 grains had been given in two days in 7½ grain doses (78). Quinidine sulphate dissolved in saline stopped an attack on the twenty-first day after 7½ grains had been injected intravenously (79); in another on the twenty-third day after 30 grains had been injected. The latter patient vomited and was unconscious for fifteen minutes (80). It will be clear that in this severe condition some risks in treatment are justifiable.

Finally, potassium chloride, gr. xv, given every four hours, in addition to quinidine sulphate, gr. vi, every three hours by mouth, succeeded in one case which had resisted other forms of therapy (81)

REFERENCES

1 Lu[illegible]
2 Lisa[illegible]
3 Sap[illegible]
4 Wo[illegible]
5 Harrison [illegible] 104, 809, 845
6 [illegible]
7 [illegible], 145.
8 [illegible]
9 [illegible]
10 L[illegible] 1103
11 N[illegible] J, 17, 85
12 S[illegible] siol, 134, 398
13 N[illegible] eart J, 26, 164
14 L[illegible]
15 Parsonnet [illegible]
16 K[illegible] eart J, 31, 74
17 De[illegible], 571.
18 Le[illegible]
19 De[illegible]
20 Ba[illegible], 20.
21 Gouley, Soloff [illegible] (1943) Amer Heart J, 25, 760
22 Cookson (1929) Quart J Med, 23, 309
23 Altschule (1939) Amer Heart J., 18, 1
24 Garvin (1942) Amer J med Sci, 203, 788
25 Tung (1936) Amer Heart J, 12, [illegible]
26 [illegible]
2[illegible]
2[illegible] J Med, 229, 360
2[illegible]
[illegible] Med, 66, 625

hydrochloride, gr. x, should be given slowly by intravenous injection, preferably under electrocardiographic control. By so doing the injection can be stopped if normal rhythm is observed to return. In long attacks in which the patient seems likely to die, the following procedures have proved successful. Quinidine sulphate, gr. iii, given every hour, slowed the rate and relieved the symptoms in one case, although it did not restore normal rhythm. Intramuscular injections of quinine bi-hydrochloride restored normal rhythm after 240 grains had been given in two days in 7½ grain doses (78). Quinidine sulphate dissolved in saline stopped an attack on the twenty-first day after 7½ grains had been injected intravenously (79); in another on the twenty-third day after 30 grains had been injected The latter patient vomited and was unconscious for fifteen minutes (80). It will be clear that in this severe condition some risks in treatment are justifiable.

Finally, potassium chloride, gr xv, given every four hours, in addition to quinidine sulphate, gr. vi, every three hours by mouth, succeeded in one case which had resisted other forms of therapy (81)

1 LUTEN
2 LISA, S
3 SAPHIR,
4 WOOD (... 104, 805, 845
5 HARRISON
6
7 ... 145.
8
... 1103
... Amer Heart J., 17, 85
... J Physiol, 134, 398
... Amer Heart J., 26, 184
... 17, 585
15 PARSONNET, MILLER, BERNSTEIN, KLOSK (1948) Amer Heart J., 31, 74
16 KATZ, ESCHELBACHER, STRAUSS (1937) Amer Heart J, 14, 571
17 DE GRAFF, BATTERMAN (1941) J Mt Sinai Hosp, 8, 476
18 LEWIS ...
19
20 ... art J, 29, 20.
21 ... t J., 25, 760.
22
23
... Amer. Heart J., 18 1
24 GARVIN (1942) Amer J med Sci, 203, 788
25 TUNG (1936) Amer Heart J ...
... Engl J Med, 229, 360
... 2, 263
... (1940), Arch ...

CHAPTER X

FAILURE OF THE HEART

This chapter deals with the subject to which most of the topics discussed in previous sections of this book are likely to lead sooner or later. During the last twenty-five years there have been many changes in ideas on the hæmodynamics of heart failure. Looking back further, over a hundred years, one is often struck by the clear insight of the Old Masters of medicine, not least among them being James Hope, so much of whose writings are firmly established to-day. The fundamental step which first put the phenomena of heart failure on a sure experimental basis was the work of Starling Since then work has progressed fast. The clinical estimation of the cardiac output, at first hampered by technical difficulties, has now become reasonably accurate by means of the method of cardiac catheterisation. The same procedure has thrown further light on variations in the venous pressure: the cause of the variations and their relationship to cardiac efficiency needs much further study. The volume of the blood, how and why it varies in heart failure, is still obscure, but no doubt very important. The rate of the blood flow can now be measured in selected stretches of the circulation The pathogenesis of œdema still needs much elucidation. This group of subjects is an active growing point of medical knowledge. The correlation of the information they give as yet is uncertain. The methods necessary are complex and highly technical Many points need full elucidation at one time and in one patient, with repetition of all investigations as clinical improvement or deterioration occur, But the results will be valuable to all. Many conclusions are still conjectural, and no doubt many will change a good deal in the near future.

The subjects considered will be the output of the heart, the venous pressure, the volume of the blood, the volume of the heart, and the rate of the circulation These may be regarded as *primary*. Secondary topics are the effects produced by derangement of

them on the lungs, as shown by changes in the vital capacity, *causing the cardinal symptom of dyspnœa*; and on the peripheral circulation causing œdema. *Cyanosis is due to several causes.* The effects on the liver and kidneys, the latter possibly of increasing importance, are next reviewed. Finally, come the clinical phenomena of the two types of heart failure, left-sided and right.

Cardiac Output

The output of the heart is a measure of the work it performs. *The estimation of the output is, therefore, of fundamental importance in the study of heart failure*

Methods. Most of the methods by which the output is obtained are based upon the *principle of Fick* (1870). If the amount of oxygen required to turn a litre of venous into arterial blood, which represents the arterio-venous oxygen difference, is known, then the *amount of oxygen consumed in the lungs per minute divided by this figure will give the minute output in litres of the right ventricle.* Since the output of the two ventricles must be approximately equal, that of the left ventricle can be assumed to be the same. By dividing the minute output by the number of beats per minute the stroke output, or the output per beat, can be calculated. *The principle, though sound in general, takes no account of regurgitating blood.* Thus in aortic incompetence, while the effective output will equal that of the right ventricle, the total output of the left ventricle includes the blood returning during diastole.

The formula of Fick is -

$$\text{Cardiac output in litres per minute} = \frac{\text{Oxygen consumption in lungs in ccs. per minute}}{\text{Arterio-venous oxygen difference in ccs. per litre}}.$$

The oxygen consumption in the lungs is obtained by analysing samples of expired air, collected in a Douglas bag. In order to find the arterio-venous oxygen difference by the direct Fick method it is necessary to obtain a sample of arterial blood by puncture, and a sample of blood from the right side of the heart, since blood returning in the different veins varies in composition. To avoid these punctures, methods have been devised using gases which are

absorbed from the lungs. Of these the *Acetylene method* of Grollman (1) has proved the most satisfactory. Acetylene is absorbed from the lungs at a known rate when corrections are made for temperature and pressure. The subject rebreathes a few times into a bag containing a mixture of air and acetylene until the gases in the lungs and in the bag are in equilibrium. A sample is then analysed and will contain a certain percentage of oxygen, acetylene, and carbon dioxide, the remainder being nitrogen. Rebreathing is continued for about fifteen seconds—the exact time is immaterial but must be less than the blood would take to circulate—and the composition of the gases in the bag is ascertained again. By a formula the number of litres of blood passing through the lungs during the rebreathing period can be calculated. The total volume of oxygen absorbed during this period can also be calculated; and this, divided by the litres of blood passing through the lungs, gives the arterio-venous oxygen difference, or the amount of oxygen in ccs. absorbed by each litre of blood in its passage through the lungs. This method, although accurate when the output is normal or low, has proved fallacious when the output is high, as some of the acetylene made a complete revolution before the end of the rebreathing period.

Cardiac Catheterization. In 1929 Forssman (2) had an ureteric catheter passed through his median basilic vein into his right auricle. Subsequently cardiac catheterization was used to introduce radio-opaque material into the heart. In 1941 Cournand and Ranges (3) left the catheter in position for an hour while making successive observations, clotting being prevented by running saline through slowly and continuously. The method was then applied to the problem of cardiac output, and the arterio-venous oxygen difference obtained in the following way (4) The arterial oxygen saturation is obtained from samples taken from the femoral artery. The wall is first rendered anæsthetic with novocaine, and the needle is left in position for a little time before blood is withdrawn. Samples of blood from the right auricle are withdrawn through the catheter and the degree of oxygen unsaturation estimated The difference between the two figures gives the arterio-venous oxygen difference The normal average figure is 45 cc. per litre. An alternative method is to assume 95 per cent oxygen saturation in the arterial blood, which equals

cardiac index allows for this, being the output in litres per minute per square metre of body surface. The normal figure is 3.1 litres. The cardiac index makes it possible to compare the output of groups of patients of different body build.

IN CARDIAC DISEASE the output is maintained at nearly normal levels until failure is advanced. With gross venous congestion it falls to about three litres per minute (10).

Patients in whom the exercise tolerance was normal were found by the acetylene method to have a cardiac index of 2.4 litres which is normal for that method, but the index steadily diminished as symptoms increased, and in congestive failure it was 1.6 litres (11).

Output in Anæmia, Emphysema, and Thyrotoxicosis. In these diseases a raised output is needed in order to supply the requirements of the body for oxygen. In severe anæmia the low oxygen content of the blood may require to be balanced by a very high output. The cardiac index increased steadily in anæmic patients [illegible]

reach fourteen litres (13). In *emphysema* the oxygen saturation of the arterial blood is diminished as a result of disease in the lungs; in *thyrotoxicosis* the general metabolism is increased, and more oxygen is needed by the tissues.

It will be noted that these are the diseases in which the speed of the circulation is increased.

Arterio-Venous Shunts. A high output is also required in several conditions associated with an arterio-venous shunt. Such are arterio-venous aneurysms, congenital cardiac lesions such as patent ductus arteriosus, and the increased vascularity of the bones in generalised Paget's disease (14).

Studies with the ballistocardiograph agree, and the term hyperkinæmia has been used to denote an output which is in excess of the normal when it has been corrected for weight (11).

In diseases which require a high output to maintain the needs of the body for oxygen, congestive heart failure may co-exist with an output level which may be double the average normal. Thus in one case of pernicious anæmia with congestive failure, the output was 13 litres (13).

195 cc. per litre, if the lungs are normal, and to subtract the figure for the blood from the right auricle (5). With this method only the vein need be punctured.

Estimation of the cardiac output by means of cardiac catheterization is liable to error in certain cases. Duplicate samples of auricular blood varied in their oxygen content up to 23 cc. of the gas in a fifth of the cases (6). It is suggested that different streams of venous blood in which the oxygen content differs may not mix thoroughly even in the auricle. The oxygen content of the expired air varied up to 20 per cent in one-quarter of the cases. The conclusion is that though the method is useful for studying groups of cases, individual estimations may prove erroneous.

Other methods include a computation based on the pulse wave velocity and the pulse pressure (7), and the use of the *Ballistocardiograph*, in which the recoil of the cardiac contraction is measured (8). The patient lies on a suspended table, which prevents movement except in a longitudinal direction. The systolic contraction, forcing blood towards the head, causes the body to recoil towards the feet. When the blood column strikes the arch of the aorta and moves downwards, the recoil is in the opposite direction. These movements are transmitted to the table and are resisted by a spring and photographed. The size and shape of the deflections obtained enable the output to be estimated. No great accuracy is claimed for the method, but neither arterial nor venous punctures are needed, nor any co-operation from the patient, beyond lying relaxed on the table.

Cardiac Output in Health

The average normal cardiac output estimated by using the auricular catheter is about five litres per minute recumbent, and four litres standing (5). This compares with four litres obtained by the acetylene method and the ballistocardiogram, and five litres by estimating the velocity of the pulse wave.

The output increases greatly with anxiety and may reach fifteen litres per minute (9). Unless the patient is relaxed, satisfactory basal readings will not be obtained. During exercise the output may increase to twenty-five or more litres per minute. The output also varies according to the size of the individual. The

The same kind of changes were found in syphilitic aortic incompetence when the right heart failure was secondary to the left.

Right Auricular Pressure. The normal pressures vary from −2 to +2 mm. Hg, or −26 to +26 mm. water. Tracings show four waves during the cardiac cycle. The first is positive and is due to auricular systole, the second is also positive and is due to the closing of the tricuspid valve. The last two are negative, the first being associated with a fall in pressure on the descent of the base of the heart during ventricular systole, and the second being due to the fall in pressure on the opening of the tricuspid valve and the consequent rush of blood into the ventricle.

In right ventricular failure the following changes occurred: a general rise in auricular pressure which may reach 20 mm. Hg. (260 mm. H_2O) or more; and a larger fall than normal in auricular pressure during the descent of the base of the heart and during the early filling phase of the ventricle.

In tricuspid incompetence the auricular pressure is higher during ventricular systole than during diastole owing to the regurgitating blood. During this phase the pressures are often higher than in the arm veins.

Venous Pressure. For clinical purposes estimation of the venous pressure must suffice.

METHODS. In the original method of Moritz and Tabora a needle with a wide bore is introduced into the vein, and sterile normal saline is run in from a graduated burette. When the point of equilibrium is reached the pressure can be read off on the burette. The pressure changes can be recorded on a smoked drum, and by using heparin the record can be continued for forty-five minutes (17). The disadvantage of this method is that a rather complicated sterile outfit is needed. To avoid this the needle may be attached to an aneroid barometer to which the venous pressure is transmitted by a column of air (18). But in either case an unpleasant vein puncture has to be done with a large needle.

Recently this difficulty has been overcome (19). A specially sensitive aneroid barometer is used, connected to a small rubber bulb which can be compressed by a screw clamp. A rubber tube leads to a narrow graduated glass tube with a small needle attached. Sterile two per cent sodium citrate solution is supplied in 1 cc. ampoules, and the contents of an ampoule are drawn into

SUMMARY. The cardiac output appears to be one of the basic functions of the body which are maintained as long as possible. With the onset of cardiac failure it may fall to 80 per cent of the patient's normal, but only in the presence of gross venous congestion does it drop to 60 per cent. On the other hand, in health it increases with anxiety, making relaxation of the patient essential for accurate readings. It increases greatly on exercise. In certain diseases such as *severe anæmia* and *thyrotoxicosis* the needs of the body for oxygen require a high output to be maintained. An output above the normal average may be actually insufficient for these cases, and may indeed be found when signs of congestive failure are present.

Venous Pressure

At the beginning of the century Starling showed that, up to the point at which the heart failed, the force of the cardiac contraction depended upon the diastolic length of the muscle fibres: this is determined by the pressure at which the heart is filled. These changes in pressure have now been recorded in the right ventricle and the right auricle, as well as in the peripheral venous system.

Right Ventricular Pressure. A catheter has been introduced into the right ventricle through the tricuspid valve, and the position verified by cardioscopy as well as by the record of altered pulsations (16). The normal right ventricular systolic pressure varies from 18 to 30 mm. Hg. The pressures at the beginning of diastole vary from −7 to +2 mm. Hg., at the end from 0 to +4.5 mm. The pulse pressure is fairly constant and averages 22 mm.

In cases of primary lung disease, such as emphysema and fibrosis without clinical signs of right ventricular failure, the ventricular systolic pressures were sometimes normal, but in most cases were moderately increased, ranging from 34 to 57 mm. The diastolic pressures were always normal. The ventricular systolic pressures were also high in all cases of primary left-sided failure.

In right ventricular failure the diastolic filling pressure increased as well. In one case of mitral, aortic, and tricuspid disease with auricular fibrillation, the right ventricular systolic pressure was 103 mm. Hg, or four times the normal, and the diastolic and right auricular pressures were 29 mm. which equals 377 mm. of water.

position than in the recumbent (20). Abdominal compression often leads to a rise in the venous pressure in early failure, whereas in normal subjects it causes a slight fall. This is due to portal congestion, and the sign of filling of the external jugular veins may at times be elicited before any general rise takes place. When the venous pressure reaches 220 mm. enlargement of the liver was always found. If it was 250 mm, ascites and œdema were also present. The reverse was not always true. Although the venous pressure was always high during increasing failure, it might become normal when the failure was receding, before anasarca and enlargement of the liver had gone (20).

CONSTRICTIVE PERICARDITIS. Both the right auricular and the venous pressures were high in constrictive pericarditis, while the right ventricular pulse pressure was 12 mm. Hg. which is one-half of the normal (16). Spontaneous changes in the venous pressure had no effect upon the cardiac output, nor had venesection, though it reduced the venous pressure by 70 mm. H_2O. The raising of the venous pressure by 150 mm. by means of a saline infusion did not increase the output (21). The conclusion was that the defect in constrictive pericarditis was the obstruction to the diastolic filling of the ventricle by a scar which could not be distended by raising the venous pressure.

In a case of pneumo-pericardium the pericardial pressure could be raised by adding air. The venous pressure was 95 mm. H_2O above the pericardial at the beginning. When the pericardial pressure reached 145 mm. the venous pressure was 185 mm., and this difference of 40 mm. was maintained until the pericardial pressure was 265 mm. At that point the difference fell to 25 and tamponade ensued in six minutes (22).

EFFECTS OF VENESECTION. The effects of venesection have been studied by right auricular catheterization with conflicting results. In one series from 300 to 900 cc. were withdrawn. The right auricular pressure fell by an average of 38 mm. H_2O, but there was no change in the cardiac output nor in the arterial pressure (23). In another in which from 400 to 1500 ccs. were withdrawn, the right auricular pressure fell but the output increased and the arterial pressure fell (24). It is possible that an element of anxiety entered into these cases. During episodes of fainting with the patient recumbent during venesection, the

Summary. The pressure changes in the right ventricle, right auricle, and peripheral veins show clearly the sequence of events in right ventricular failure, whether this be primary, or secondary to left ventricular weakness. The first changes to be observed, as a result of the raised pressure in the pulmonary circuit, is an increase in the ventricular systolic pressure. At this stage the ventricular diastolic pressure, the right auricular and venous pressures are normal. As the ventricle weakens, the diastolic and filling pressure rises, and the pressure rises also in the right auricle and in the peripheral veins. As the ventricular failure progresses the pressures rise more and more, but the difference between the venous and the right auricular pressures becomes progressively less. In health this difference is about 100 mm. H_2O; in advanced failure there may be no difference at all, and the right auricular pressure may even exceed that in the arm vein in certain phases of the cardiac cycle. This causes stagnation in the vein and reversal of flow at times; then the pressure changes in the right auricle are transmitted as pulsations to the veins.

Blood Volume

Methods. The volume of the blood can be obtained by injecting intravenously 6 cc. of Evans Blue dye. Samples of venous blood are taken from twenty to sixty minutes later and the mean dilution of the dye estimated by a photo-electric colorimeter after the plasma proteins have been removed (27). The blood volume can then be calculated. The blood volume varies with the height and sex of the individual, but normal values have been worked out (28) and the results in heart failure can be expressed as a percentage deviation from the predicted normal. The method is probably accurate to within 10 per cent (29), but there are several possibilities of error.

Another method uses "labelled" red cells (30). Six cc. of blood are taken from the patient and mixed with radio-active phosphorus. Three cc. are injected into the vein of one arm, and specimens are withdrawn from a cannula inserted into the brachial artery of the other arm. The radio-activity of the specimens, when equilibrium has been attained, compared with that of the original moiety not injected, enables the dilution to be calculated, and so the total amount of circulating red cells can be estimated.

right auricular pressure rose slightly. The conclusion was that the whole syndrome of syncope, including the nausea and sweating, was due to vagal stimulation (23).

Clinical Observations. Lewis (25) has given a full account of the grades of venous engorgement in the neck and how they may be recognised. Normally all veins that lie above the level of the manubrium sterni are collapsed when the patient is not lying flat, unless the flow of the blood in them has been obstructed. In the supine position the root of the neck will be below the manubrium level, and the external jugulars can be made out until they collapse about one-third of the distance to the angle of the jaw. In order to make sure that the vein is collapsing and is not being lost owing to its taking a deeper course, it should be obstructed by light pressure on it at the root of the neck. It will then fill throughout its length.

In venous engorgement the swelling will be visible beyond the middle of the sternomastoid, or even to the jaw. If the pressure is high, the veins will remain swollen when the head and shoulders are raised off the bed. The neck should be freed from clothes, and should be moved slightly from side to side to eliminate any pressure from the deep fascia of the neck.

The maximum venous pulsation occurs at the point where the vein is collapsing. Neither collapsed nor grossly distended veins can pulsate. Jugular pulsation may be distinguished from carotid pulsation by the absence of the sharp arterial thrust. Normal venous pulsation occurs at the root of the neck when the patient is lying flat. If the veins are overfull, pulsation may be observed as far up as the jaw. If the venous pressure is much increased, no pulsation will be seen in the supine position, but it will be evident when the patient is sitting upright. This is due to the force of gravity which in the erect position has lowered the pressure in the jugular veins, so that they collapse at a point in their course through the neck.

The veins under the tongue are both easy to see and reliable as an index of raised venous pressure. The tongue is about 200 mm. above the right auricle when the patient is sitting upright. Since the upper limit of the normal venous pressure is 150 mm, they should be collapsed. Distended veins under the tongue in the sitting position indicate considerably raised venous pressure (26).

volume to remain in circulation. The initial fault seems to lie in the inability of the kidneys to excrete sodium. The volume of the blood increased when normal subjects were given large quantities of salt for a week. Their venous pressures rose and so did their weight (34). A group of patients who had recovered from heart failure had 10 g. of sodium chloride added daily to their diet. The heart accelerated by an average of fifty beats; the venous pressure rose, the time of the circulation was prolonged, and the weight increased; the vital capacity fell. A state of congestive failure was produced. Restoration of the basic diet caused some improvement, but full doses of digitalis were required before the patients regained their former state (35). Another series of patients, whose failure had been controlled by digitalis and low salt diet, was given 24 g. of sodium chloride intravenously (36). The excretion of sodium and chloride in these patients was found to be only 20 per cent of that in cases with asthma and nephrosis who were used as controls. A mercurial diuretic led to increased excretion of sodium and chloride. It has been found that the reduction in blood flow following a decrease in the cardiac output affected the renal blood flow more than the rest of the circulation (37) Normal subjects could excrete 1.2 per cent of the sodium filtered; in cardiac failure 0.02 per cent was excreted. Whatever the cause, the raised blood volume in heart failure is definitely associated with retention of sodium by the kidneys.

Not every case with congestive failure and raised venous

[illegible] litres (18). In acute failure the raised venous pressure may be due to spasm of the veins (10). Alternatively it may be caused by incomplete emptying of the right ventricle (38)

Summary. The volume of the blood is usually raised in cardiac failure. The increase is associated with an inability of the kidney to excrete salt. There is no evidence as to whether the increase in the volume of the blood causes the rise in the venous pressure or is the result of it; but adding salt to the diet of patients who had recovered from heart failure led to an increase in venous pressure, as well as a return of *œdema*. Whether the retention of sodium is due to a primary deficiency of the kidney following a

When the volume of the packed red cells is known, the plasma volume can be obtained by means of the hæmatocrit, and the sum of the two is the blood volume. The results by this method are lower than by the dye method and are claimed to be more accurate.

In severe anæmias the blood volume can be obtained by giving a transfusion of known quantity and known hæmoglobin content. There must be no loss of plasma during the time of the test (31). Up to 500 ccs. of blood with a hæmoglobin content of from 110 to 170 per cent are given rapidly. The hæmoglobin value is estimated before and after transfusion, that of the transfused blood is known already. The blood volume is calculated from the formula :

$$\text{Blood Volume} = \frac{\text{Volume of transfused blood (Hb of transfused blood minus Hb after transfusion)}}{\textit{Hb after transfusion minus Hb before transfusion.}}$$

Results. THE NORMAL BLOOD VOLUME varies from 3 5 to 5 litres with the red cell method, with an average of about 70 cc. per kilogram of bodyweight With the dye method the figures are rather higher. In heart disease without failure the blood volume is normal The volume was estimated immediately after exercise in normal subjects and in those with heart disease, and was found to be decreased in each group (32). Both venous and arterial pressures were raised. The figures had returned to normal in twenty-five minutes The decrease in the volume of the blood was attributed to the passage of fluid into the interstitial spaces and to the active muscles.

IN CONGESTIVE FAILURE the volume of the circulating blood is greatly increased, to an average of 40 per cent in one series (29). But the results were variable and could not be correlated with the height of the venous pressure or of the circulation rate.

The reason for the increase in volume of the blood is not altogether clear. The rise may take place before there is any change in venous pressure, and is due at first to dilution of the blood by retention of fluid (33). Later more plasma protein is formed and the formation of red cells presumably increases. When œdema ensues, the increased pressure of the extracellular fluid, as well as the increased protein in the plasma, allows a larger

volume to remain in circulation. The initial fault seems to lie in the inability of the kidneys to excrete sodium. The volume of the blood increased when normal subjects were given large quantities of salt for a week. Their venous pressures rose and so did their weight (34). A group of *patients* who had recovered from heart failure had 10 g. of sodium chloride added daily to their diet. The heart accelerated by an average of fifty beats; the venous pressure rose, the time of the circulation was prolonged, and the weight increased; the vital capacity fell. A state of congestive failure was produced. Restoration of the basic diet caused some improvement, but full doses of digitalis were required before the patients regained *their former state* (35). Another series of patients, whose failure had been controlled by digitalis and low salt diet, was given 24 g of sodium chloride intravenously (36). The excretion of sodium and chloride in these patients was found to be only 30 per cent of that in cases with asthma and nephrosis who were used as controls. A mercurial diuretic led to increased excretion of sodium and chloride. It has been found that the reduction in blood flow following a decrease in the cardiac output affected the renal blood flow more than the rest of the circulation (37). Normal subjects could excrete 1.2 per cent of the sodium filtered; in cardiac failure 0.02 per cent was excreted. Whatever the cause, the raised blood volume in heart failure is definitely associated with retention of sodium by the kidneys.

Not every case with congestive failure and raised venous pressure has an increased blood volume. In severe anæmia the right auricular pressure may be raised, although the blood volume is as low as 2.7 litres (13). In acute failure the raised venous pressure may be due to spasm of the veins (10). Alternatively it may be caused by incomplete emptying of the right ventricle (38)

Summary. The volume of the blood is usually raised in cardiac failure The increase is associated with an inability of the kidney to excrete salt. There is no evidence as to whether the increase in the volume of the blood causes the rise in the venous pressure or is the result of it; but adding salt to the diet of patients who had recovered from heart failure led to an increase in venous pressure, as well as a return of œdema. Whether the retention of sodium is due to a primary deficiency of the kidney following a

falling cardiac output, or to some other factor, is not at present clear. The recent demonstration of a dual circulation in the kidney may throw light on this subject.

Heart Volume

Interesting work on this subject has been performed by Nylin and his associates.

Methods. Two simultaneous teleradiograms are taken at right angles to each other, an accurate centering of the tubes having been attained. The volume can then be calculated from the following formula :

Volume = 38 × longitudinal × transverse × sagittal axis.

In seventy normal subjects the volume of the heart varied from 180 to 970 cc., or from 7 to 13 cc. per kg. of body weight ; or from 250 to 500 cc. per square metre of body surface (39).

In patients dying of congestive failure estimations by this method were made shortly before death and again after death. The total volume of the heart was then ascertained at autopsy by the displacement method, and the amount of blood in each chamber was also measured (40). The estimations made after death agreed surprisingly well with the figures obtained at autopsy, but the volume estimated during life was sometimes much greater; presumably some of the blood had drained out of the heart after death.

Cardiac Dilatation and Heart Volume. When there is clinical enlargement the total volume, of course, increases; but the point is made that a great increase in volume is sometimes largely due to an increase in capacity with an excess of blood in the chambers. In some cases this was enormous. On one occasion 1065 cc. of blood was removed from the heart at autopsy; in another case the amount of blood in the heart during life was estimated to be 1750 cc. (40). Since the cardiac output in congestive failure is unlikely to be more than four litres a minute, this residual blood in the heart would take from fifteen to twenty-five seconds to move on, and might take longer. The blood flow, therefore, must receive a distinct check in the dilated heart.

Circulatory Rate

The speed of the circulation varies according to the cross section of the bed. It is fastest in the arteries, decreasing gradually towards the periphery. It is slowest in the capillaries: in the veins the speed increases as the blood approaches the heart. Direct observation of the speed in the different sections is impossible in man, but many methods have been devised consisting in the introduction of some substance into one point of the circulation, which can be recognised as it arrives at another. In nearly all the tests the arm vein is used for the injection of the substance, which is recognised as it reaches the brachial artery at the other side, or the arteries or capillaries of the head. Thus the whole of the pulmonary circulation is included with varying portions of the systemic. Exceptions are tests in which the substance is recognised as it reaches the heart or lungs, or when it is inhaled.

Radium Emanation. This was the first method to be described (41). A radio-active solution of sodium chloride is injected into the vein and its arrival timed by stop-watch at the other brachial artery, where it can be seen on a special detector. By placing the detector over the right auricle the arm to heart time can be ascertained. The normal arm to arm time varies from fifteen to twenty seconds with an average of seventeen seconds. The arm to heart average time is seven seconds. In children from two to twelve years the average arm to arm time is eleven seconds; in infants it is seven seconds (42)

The radium test is objective, requiring no co-operation from the patient. It is probably quite accurate, but the apparatus is elaborate and costly, and unsuitable for general use. Other objective methods include the fluorescein, histamine and cyanide.

Fluorescein. Five cc. are injected and the lips are observed in the dark under ultra-violet light. They turn green-yellow when the dye reaches them. The normal limits are from 15 to 20 seconds, the greater number being between 15 to 17 seconds (43).

The histamine method registers the time from the arm vein to the capillaries of the face, and the end point being a flush, so that it includes a larger portion of the systemic circulation than any other test; 0 001 mg. of histamine phosphate per kilo of body weight in a 1 : 10,000 solution is injected (44). A convenient way

The ether and amyl nitrite tests together include approximately the same length of the circulation as the histamine. Allowing for the time taken by amyl nitrite to reach the alveoli and be absorbed, the combined time of 23.5 seconds agrees well with the twenty-three seconds of the histamine test.

Abnormal Circulatory Rates. The speed of the circulation is increased in severe anæmia, thyrotoxicosis, and to a less degree in emphysema. These are the conditions in which the cardiac output is high. A small but progressive increase was found after the third month of pregnancy (51). The rate becomes slow in myxœdema and polycythæmia.

HEART DISEASE WITHOUT SYMPTOMS. The rate of the circulation may be normal or slightly slowed. A relation has been observed between the volume of the heart and the rate of the circulation so that a prolonged time would indicate that the heart is dilated (52). There is also some evidence that the substance may be diluted by the residual blood in very large hearts. When "labelled" red cells were being used to determine blood volume, several minutes elapsed before equilibrium was attained when the rate of the circulation was slowed, whereas it occurred in about one minute when it was normal (54). In patients with large hearts but no symptoms, the taste with decholin may persist for a minute or more, although the onset is only slightly delayed (40) suggesting that some of the drug lingers in the heart.

CARDIAC FAILURE. The rate is always slow. The slowing may amount to sixty or more seconds, which is about thrice the normal time. Much of the slowing takes place in the pulmonary vessels, and a close relation exists between the speed of the circulation and the vital capacity (43). The arm-to-heart times which register the speed in the veins, may be normal in cases where the left ventricle is primarily at fault, while the arm-to-arm times, which include the pulmonary circulation, are considerably prolonged (41). When the venous pressure is raised, the speed in the veins decreases.

On the other hand, the speed of the circulation bore also a close relation to the size of the heart in patients with congestive failure (29). A considerable slowing of the flow in the heart would account for the grossly prolonged times sometimes found, which are out of all proportion to the abnormalities recorded by other methods

venous pressure does not keep pace with the rise in pressure in the heart. The difference in pressure becomes progressively less until the stage is reached where the pressure in the right auricle and in the right ventricle in diastole is equal to that in the veins. It may even be greater, resulting in a reversal of flow during parts of the cardiac cycle. This strongly suggests that the primary cause of the rise in venous pressure lies in the heart itself; the increased venous pressure maintains the onward flow of blood into the heart. The necessary increase in venous pressure can be secured either by constriction of the veins causing a narrowing of the venous bed, or by an increase in the blood volume.

Starling (56) noted constriction of the arteries with dilatation of the arterioles and pooling of the blood in the veins. Recently constriction of the veins has been postulated (10). Whether the constriction was in the arteries or in the veins, the narrowing of the bed, which may possibly be effected by the adrenals, would increase the pressure in the veins near the heart. On the other hand, a larger volume of blood in circulation could be accommodated in the veins, and so would raise the venous pressure. This was, in fact, found to be the case in normal subjects whose blood volume has been increased by excessive ingestion of salt. Both factors may operate in different cases, and the constriction of the veins may be the first mechanism to be invoked, followed later by the hæmo-dilution which leads to increase in the volume of the blood.

An increase in the blood volume is also needed [illegible] the [illegible] -ten- [illegible] the [illegible] through them.

The cardiac output during this time seems to remain at nearly normal levels. It must be remembered that estimations of the output are only accurate if the patient is relaxed, and relaxation may not always be easy to secure with a catheter introduced into a vein in the arm, and a needle in the femoral artery.

The process continues *until* the muscle fibres are stretched beyond their optimum length. By this time the residual blood in the heart may be very great, accounting partly for the gross slowing of the circulation rate. Further dilatation of the heart brings weaker contractions and the output falls. At this stage the

of investigation. Dilution of the substance by the blood in the heart would also account for the difficulty in obtaining a satisfactory end point in cases showing a slow rate by the histamine, amyl nitrite, or decholin tests.

Summary. Many tests are now available which time the speed of the flow of the blood over certain portions of the circulation, most of which include the whole of the pulmonary circuit. In patients without failure the times are either normal or slightly prolonged, depending upon the size of the heart. In cardiac failure the speed is always reduced, and the time may be grossly prolonged. When the venous pressure is normal, as in left ventricular failure, the slowing takes place in the pulmonary vessels, and a check occurs also in the heart, when the venous pressure is raised in right ventricular failure, the flow in the systemic veins is retarded.

Conclusions

When the heart begins to fail, three major changes take place. The cardiac output falls a little, the venous pressure rises, the blood volume increases. The relative times of onset of these changes are very variable and any one may precede the other. The circulation also slows, but most of the tests employed are not sufficiently precise to make small changes of much significance.

Experimental work with the heart-lung preparation has shown that the first change to be observed is a slight increase in the systolic volume of the heart. Owing to a diminished stroke output, the ventricle does not empty itself completely. The next change is an increase in the diastolic volume of the ventricle, since nearly the same amount of blood returns from the veins and has to be accommodated in addition to the blood that is not expelled (55). According to Starling's law, the increased diastolic ventricular pressure would stretch the fibres and lead to an increase in the stroke output, if the heart was capable of responding, and the circulation would then regain efficiency. This sequence probably occurs in health at the beginning of exercise. In cardiac failure a permanent increase in the diastolic ventricular pressure takes place, at first probably during exercise only, later at rest. The problem arises as to how this is brought about.

Cardiac catheterization has shown that the rise in the peripheral

An increase in the respiratory rate is produced when the leg of a dog, severed from the body save for the sciatic nerve, is stimulated to muscular activity. Muscular activity alone, therefore, can accelerate the rate of breathing. Increase in the pressure in the great veins near the heart, or in the right auricle, stimulates the respiratory centre. Perfusion of the lungs and distension of the lung capillaries will stimulate respiration. In all these reflexes the vagus is the efferent path, for they are abolished when it is cut (57). The reflexes are all linked with the general rise in venous pressure which takes place at the beginning of exercise. In health the circulation is adjusted to the needs of the body by a rise in the cardiac output which may reach thirty or more litres per minute. The diseased heart is unable to accomplish this increase in the output and there is evidence that the rise in venous pressure is greater and more prolonged in patients with heart disease than in normal subjects It may be associated with the inability of the heart to empty itself completely.

Increase in respiratory activity may be caused by changes in the hydrogen ion concentration in the blood towards acidity, by diminished oxygen saturation in the arterial blood, and by an increase of carbon dioxide saturation at the respiratory centre. In uncomplicated cardiac failure these remain normal until near the end, and the increase in respiration appears to be due solely to the raised pressure in the systemic veins and in the pulmonary circulation.

DIMINISHED VITAL CAPACITY. *The* vital capacity is the maximal amount of air that can be expelled from the lungs after the maximal inspiration. The air is exhaled into a spirometer and the figure is read on a graduated scale. The result must be standardised against the volume which is normal for the body surface of the individual. This may be done by using the linear formula of Du Bois, and the result multiplied by 2,500, or more simply, by taking twenty-five times the height in centimetres in men, and twenty times in women as the factor.

The vital capacity *varies* with physical fitness and increases with practice. The normal average in males is 4,600 cc. (59). It is decreased in obesity, pulmonary disease, thyrotoxicosis, and neuro-circulatory asthenia. *In* cardiac failure it may fall as low as 1,000 cc.





PLATE 26

Congestion of Pulmonary Veins
in heart failure due to hypertension.

The figure representing the vital capacity gives mathematical expression to the fact that in congestive failure the patient is unable to take a deep breath. Dyspnœa, in fact, varies inversely as the vital capacity and directly as the degree of ventilation. We must now consider why this is so.

PULMONARY CONGESTION. It is reasonably certain that the pressure in the pulmonary veins rises in cases of left ventricular failure or of mitral stenosis. The systolic pressure in the right ventricle and pulmonary artery increased from the normal 30 mm. Hg. to 70 mm. in left ventricular failure, and rose to 104 mm. in a case of mitral stenosis (16). The circulation rate in the lungs is slowed, and, though some of the slowing is related to the amount of residual blood in the heart, much takes place in the pulmonary circuit and indicates stasis in the vessels. Engorgement of the pulmonary vessels can be seen in the enlargement of the shadows of the lung roots in skiagrams of patients with left ventricular failure (Plate 26). Engorgement of the pulmonary circulation stimulates respiration. Congested vessels impair the elasticity of the lungs, so that there is a lack of distensibility. At the end of expiration the pressure in the pleural sac may be positive; as a result of this, inspiration will require more effort to overcome it. The end of the story is to be seen in the "brown induration" found at autopsy. The lungs are stiff, hard, inelastic, and sections show turgid capillaries in thickened alveolar walls.

Summary. Cardiac dyspnœa is due to the combination of two factors, a call for increased ventilation, and the inability to breathe deeply in response. The first is due to reflexes arising as the result of the increase in venous pressure on exertion: the second to changes in the pulmonary circulation. As heart failure advances, the venous pressure becomes permanently raised, the pulmonary changes progress, and the patient becomes orthopnœic

Orthopnœa. In the later stages of cardiac failure the patient is short of breath even at rest, and cannot lie flat in bed. The number of pillows required at night is a rough, but useful, guide of the degree of orthopnœa present. A recent increase in the number shows progressive cardiac failure. Finally, the patient may have to lean forward supporting his head on a bed rest, or spend his night in a chair.

The ease obtained on sitting up is due, first, to the fall in the venous pressure, which is on the average eighty mm. H_2O lower in the sitting position (20), since increased venous pressure stimulates the respiratory centre reflexly. The cardiac output also falls by about a litre. Secondly, the vital capacity is increased, for the upright position is the best for making use of the accessory muscles of respiration. The spine must be straightened in order to increase the capacity of the chest. Thirdly, the effect of upward pressure on the diaphragm by an enlarged liver is reduced to a minimum.

ACUTE PAROXYSMAL CARDIAC DYSPNŒA. We have seen how progressive liability to dyspnœa on exertion marks the downward progress of the patient with heart disease. In the more severe grades of disability, particularly if the cardiac efficiency has deteriorated rapidly, whether the acute phase of failure has been precipitated by a sudden excessive demand such as over-exertion, or, sometimes, by a sudden myocardial weakness such as infarction, the emergency is marked by an acute paroxysm of dyspnœa. Occasionally this happens in mitral stenosis during pregnancy. The underlying cause is the development of severe engorgement of the pulmonary circulation. This engorgement arises most commonly of all in the recumbent posture, and these are the attacks which occur during sleep. But they may be precipitated by undue exertion during the day.

Allbut has left us a graphic account of a severe attack: "The patient, seized and throttled before he could cry out, sprang up had to wrestle with death. The desperate conflict made the fell enemy almost visible to us. Now this way, now that, springing up in bed to fight from the edge of it, to sink back in utter exhaustion, but only to rise again panting, with the sweat streaming from him, desperately to renew the battle, the scene was almost as distressing to the bystanders as to the victim."

NOCTURNAL DYSPNŒA. Patients with much pulmonary congestion, due to failure of the left ventricle under the burden of hypertension or aortic valvular disease, or with severe ischæmic lesions of the left ventricle, are liable to suffer from acute *nocturnal dyspnœa*. The attacks usually occur in the middle of the night. The patient is awakened after an hour or two of sound sleep by a feeling of imminent suffocation, which causes him to spring up panting for breath. He may sit up in bed or get out to go to a



PLATE 27

Acute Pulmonary Œdema in Hypertension.

The rise in pressure in the ... a reflex, and certainly overloads the ventricle. Stimulation of the cardiac end of the cut vagus caused bradycardia, and produced œdema. Of the drugs that were tested, adrenalin produced œdema; but hypnotics, such as morphia and chloral prevented it.

Acute pulmonary œdema is a very hazardous state; unless the congestion abates the patient may drown in the œdema.

Ætiology. The dominating cause in the nocturnal attacks seems to be postural; the patient slips down in bed during sleep. In the recumbent posture the venous filling pressure is higher and the output greater. Breathing is less easy. Difficulties then arise during sleep which reach a degree of acute embarrassment and the patient awakes with a start and the attack begins. Exciting causes, or "triggers," may be a paroxysm of coughing, dreams, abdominal distension, discomfort of the urinary bladder. Too much activity during the preceding day may play a part.

Some patients cannot lie on the left side or on the back without dyspnœa or angina. Sometimes lying on the right side brings on the dyspnœa. Attacks can be stopped by turning over in bed. This form of postural dyspnœa has been termed *trepopnœa*. They are probably commoner than one might suppose (60).

SLEEP STARTS. These attacks occur as the patient drops off to sleep They are associated with Cheyne-Stokes respiration. "Respiration rare and large, with long intervals, afterwards becoming short." (Hippocrates.) The period of apnœa is followed by sudden increasingly deep inspiration which awakes the patient. Thus Cheyne-Stokes breathing tends to disappear as sleep deepens. It is probably due to uneven stimulation of the respiratory centre, which later becomes more steady as the tension of the CO_2 in the blood rises. "Many years ago I had an opportunity of seeing a number of these cases and observed that before they went to sleep they had a tendency to Cheyne-Stokes breathing, and in one or two cases the attacks came on at the end of apnœa." (Mackenzie.) These attacks are easily controlled by an intramuscular injection of cardophylin (0.48 gm.) which abolishes the Cheyne-Stokes respiration for a time (61).

BRONCHOSPASM. In some cases there is the added complication of bronchospasm. It seems desirable to restrict the term "Cardiac asthma" to these. Hitherto this name has been used more or

window for more air If he is observed during the height of the attack, he will be seen to be pale, anxious, with a cold perspiration, and to have a laboured respiration. Inspiration is grunting and short, expiration is prolonged. Cyanosis will be present if the attack is severe. The pulse is rapid. Both the systolic and the diastolic blood pressures will be found to be raised, sometimes they are very considerably above the usual levels for the patient. The pulmonary second sound is loud The attack may be over in a few minutes, but, if severe, it may persist for an hour At the end of a short attack a little thick mucus, sometimes blood-stained, is coughed up At the end of a long attack the lungs may become œdematous, and the condition may pass into that of acute pulmonary œdema Otherwise, nothing more than a few moist rales will be heard on auscultation at the bases The upper lobes may be hyper-resonant.

If the failure progresses and the engorgement increases the difficulty in breathing will be complicated by the development of œdema

ACUTE PULMONARY ŒDEMA The œdema begins at the lung bases and spreads upwards The patient is cyanosed, the breathing is laboured Fine rustling crepitations are audible over the parts of the lung affected The blood pressure is high In severe attacks the patient then becomes more restless and cyanosed, and a cough begins, dry at first, later accompanied by a profuse watery, pinkish, frothy expectoration At this stage the chest is full of bubbling rales, and the pulse is rapid and feeble Skiagrams show a general lack of translucency over the lung fields, which appear quite dark on screening (Plate 27) Pulmonary œdema has been brought on by too rapid transfusion or by saline infusion (65) The vital capacity fell, the lung fields became less translucent, the vascular shadows became denser The heart increased in size, and patients felt constriction in the chest

Experimental work has suggested that reflexes originating in the carotid sinus may engender acute œdema of the lungs Perfusion of blood into the carotid artery caused pulmonary œdema in 90 per cent of dogs, but an equal volume when given into a vein did so only in 30 per cent (67) Saline did not have the same effect. Blood-letting during the infusion prevented the œdema, as also did denervation of the carotid sinus before the infusion.

is probably quickest and most effective of all. Cardophylin (0.28 gramme), given intravenously, is particularly valuable when there is bronchospasm. It is obviously safer than adrenalin, for these patients are often hypertensive. Venesection is particularly useful when there is acute pulmonary œdema. In normal subjects the vital capacity increases after venesection (66). It seemed the volume of blood in the lungs was reduced as a result; possibly the pulmonary circulation may act as a reservoir for blood which may contract in certain circumstances.

Intravenous digoxin may also find a place. Both this and cardophylin reduce venous pressure, and there may be other effects on the myocardium and coronary circulation

PROGNOSIS "Practically every case that I have seen when the patient woke up in the middle of the night suffering from great distress in breathing has died within a couple of years of its onset." (Mackenzie.)

OXYGEN DEBT. When a normal person uses his muscles, the glycogen in them is changed into lactic acid. Four-fifths of this lactic acid is normally resynthesised into glycogen. The remainder is oxidised to CO_2 and water. Most of this oxidation process goes on after the exercise, the acid being "buffered" by the tissues; hence the need for more oxygen after exertion. The extra amount required is spoken of as the "oxygen debt" which has to be paid to the tissues to enable the surplus lactic acid to be oxidised.

The oxygen consumption per minute through the lungs can be measured by a Benedict spirometer and expressed as a percentage deviation of the Basal Metabolic Rate. Tests were done after exertion in normal subjects and in patients with cardiac, pulmonary, and cardio-pulmonary disease, classified in groups according to the severity of their condition Although wide variations occurred, the B.M.R. progressively increased through the groups. The increase was roughly parallel to the fall in the vital capacity. It is suggested that a B.M.R of +20 per cent after exercise should be regarded as the limit of the normal. In patients with cardio-pulmonary disease the figure may rise above +70 per cent (68). This large increase is due to the low oxygen saturation of the arterial blood in these particular cases, which may fall as low as 35 per cent (69).

the renal blood flow was only a fifth of the average normal, so that the blood in these circumstances seemed to be diverted from the kidneys. On the other hand normal subjects who ate an excess of salt gained weight but their venous pressures also rose (31). The same effects were noted when digitalis was withdrawn in cases of rheumatic heart disease and auricular fibrillation (72). It would seem that the retention of salt is due to a diminished flow of blood through the kidneys, but that the consequent increase in the volume of the blood leads to a rise in the venous pressure which itself can cause œdema.

DIMINISHED PLASMA PROTEINS. In nephrosis and nutritional œdema the cause lies in a fall in the colloid osmotic pressure through loss of the plasma proteins. In cardiac œdema the plasma proteins are sometimes reduced and the reduction in albumen may reach 25 per cent (73), thus aiding in the development of œdema.

The protein content of œdema fluid varies from 0.1 to 0.5 per cent (71). This comparatively low figure does not favour the idea that increased capillary permeability causes œdema (74). However, after clinical œdema has gone, the average extra-cellular fluid volume may still be 50 per cent above the normal (38). This is probably because some of the plasma proteins leak out and are removed slowly, thus hindering re-absorption of water (75).

The presence of œdema interferes with the nutrition of all the tissues involved. Studies with the plethysmograph show that in unilateral œdema the blood flow is greater on the œdematous side. In bilateral œdema without heart disease the flow is faster than normal, in cardiac œdema it was still within the normal range (76). The oxygen content of the blood in the femoral vein, when gross œdema is present, may be higher than normal (77). This is because the œdema fluid acts as a barrier to the diffusion of oxygen. Diminished oxygen tension in the tissues then results. It is certain that the presence of gross œdema is bad for the individual improvement is almost always obvious when it has been got rid of From the point of view of therapy all efforts should always be made to remove œdema.

Conclusions. Œdema is due to a fall in the difference between the level of the colloid osmotic pressure of the plasma, which keeps the fluid in the capillaries, and the level of the pressure at the venous end of the capillary. Should the venous capillary pressure

that matters Hence cyanosis cannot occur in severe anæmia with hæmoglobin values below 30 per cent, whereas it is the rule in polycythæmia.

Cyanosis is seen best in those parts which are exposed to the weather such as the lips, cheeks, ears, and hands, since the subpapillary venous plexuses are most highly developed in them. The value of cyanosis as an index of cardiac disease is limited by the fact that it occurs both in health, and in diseases of other systems, Cold diminishes the rate of flow through the capillaries because the arterioles are constricted. But the capillaries are dilated and [illegible] blood

[illegible] in four conditions.

Pulmonary Disease. When pulmonary disease affects the heart the oxygen saturation in the arterial blood may fall from the normal 95 per cent as low as 35 per cent, (62) since the pulmonary disease interferes with the oxygenation of the blood. There is also often polycythæmia Cyanosis in these cases may be deep.

Mitral Stenosis Pulmonary congestion, with a slowing of the blood flow, is due to the obstruction to the exit of the blood from the lungs. Cyanosis may occur early, before the onset of failure.

Cardiac Failure. Raised venous pressure results in a slowing of the flow back from the periphery to the heart. Pulmonary congestion due to advanced left ventricular failure interferes with the oxygenation of the blood. Cyanosis is masked locally by the presence of much œdema.

Congenital Heart Disease. In some types of congenital heart disease, notably in the Tetrad of Fallot, a mixing of venous and arterial blood takes place. In others when there is a defect of the auricular or ventricular septum, a venous arterial shunt will occur when the pressure in the right ventricle exceeds that in the left. Clubbing of the fingers and toes is associated with cyanosis in congenital heart disease (p. 38).

Hepatic Engorgement. The liver is a convenient reservoir for blood that cannot be sent on fast enough by the right side of the heart. The nutmeg liver of chronic venous engorgement, with atrophy at the centre of the lobule, and fatty degeneration at the periphery, is familiar to all. Although a slight excess of bilirubin

reach within 2 mm. Hg of the osmotic pressure, or exceed it, fluid will pass out into the subcutaneous spaces. The usual change is a rise in the capillary pressure, though occasionally there is a slight fall in the osmotic pressure: but a high osmotic pressure may prevent œdema even when the venous pressure is high. Normally the raised venous pressure is associated with an increase in the blood volume, though cases have been recorded in anæmia where the blood volume was low (13). In these latter cases the plasma proteins may have been low, and so helped to cause œdema.

Pleural Effusion. Hydrothorax is common in cardiac failure, although cardioscopy is often required to detect it. It was present in 38 per cent of one series of 350 cases (78). When the rhythm was normal the incidence on the two sides was about equal, but when the auricles were fibrillating it was four times more frequent on the right side than on the left. Interlobar effusions were found in 3 per cent and were also usually on the right side. The great majority of effusions secondary to cardiac failure are comparatively small, and it is seldom that they require to be aspirated. They occur as a complication of pulmonary congestion in left ventricular failure, or in mitral stenosis. It is possible that the high incidence of right-sided effusions in patients who are fibrillating are due to the association with mitral stenosis, and that the right auricle presses on the right lung root (78).

The effects of aspiration of pleural effusions of different types have been studied (79). The venous pressure fell even though it had previously been normal. There was a small increase in the vital capacity, but no change in the cardiac output nor in the circulation time. It is well known that the effusion causes the lung to collapse: after removal the diaphragm rises, and the vital capacity does not return to normal for some time until the lung has re-expanded. In cardiac failure, however, a pleural effusion of any size should be removed early, as clinical experience shows that it is a serious embarrassment to a failing heart and to the respiration.

Cyanosis. Cyanosis is due to the amount of reduced hæmoglobin in the blood. The veins usually contain about six volumes per 100 cc. If the percentage in the capillaries reaches 6.7 volumes per 100 cc. they will have a cyanotic colour like venous blood. The percentage of reduction of hæmoglobin is unimportant; *it is the absolute amount* of reduced hæmoglobin

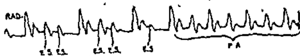


Fig. 78
Alternation of the pulse following a bout of extrasystoles
P A = pulsus alternans

... a premature contraction causes alternation to appear ... paroxysmal tachycardia ... graphic tracings of the radial pulse (Fig. 78). It may be detected by the sphygmanometer easily if the pressure in the bag *is allowed to fall slowly* as the beat first comes through. Records of the apex beat do not always agree with the pulse. Sometimes there is no alternation over the apex; in other cases the *stronger* apex thrust coincides with the weaker pulse beat. Occasionally alternation in the voltage of the R waves can be seen, in the electrocardiogram (Fig. 79)

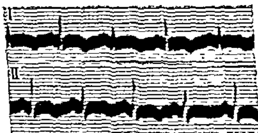


Fig 79
Alternation in voltage of R and T waves

Alternation of the heart beat occurs firstly when an apparently *healthy muscle is greatly overburdened, as in paroxysmal tachycardia*, or flutter. Secondly, when the rate is not fast *but the* heart muscle is much diseased. It is most commonly seen in patients with high blood pressure when the *myocardium* is beginning to fail. It is also met with in old people, in whom there is disease of the coronary arteries, angina pectoris or cardiac asthma. Its presence would appear to indicate exhaustion of the muscle.

Nature of Alternation. In alternation all the fibres of the heart do not contract at each systole The fibres which fail to contract may be diffused throughout the muscle, or more may fail in one

in the blood is common after prolonged venous congestion (80) frank jaundice is rare. *Jaundice is congestive failure is usually* due to the absorption by the liver of pigment from infarcts in the lungs, which may be unsuspected, or to the presence of cirrhosis.

RENAL CHANGES. The part played by the kidneys in the production of the increased volume of the blood and of œdema has already been discussed. *It may be that they are especially sensitive* to any reduction in the cardiac output. In hypertension the kidneys are affected by *the arteriolar constriction* probably in greater measure than the other internal organs, and the arteriosclerotic kidney with obliteration of many glomeruli results. When venous congestion supervenes, this may lead to a renal breakdown with raised blood urea, and the patient may die in uræmia. *In other types of heart disease the albuminuria of cardiac* failure clears up as the circulation improves. The urine is concentrated, deep in colour, with high specific gravity.

Left Ventricular Failure

In lesions such as hypertension and aortic valvular disease the strain affects primarily the left ventricle. The incidence of coronary sclerosis, too, falls particularly upon the left ventricle. In these conditions left ventricular weakness develops first. The result is pulmonary congestion due to the increased pulmonary pressure, and a slowing of the blood flow in the pulmonary circuit. This shows itself clinically by congestion at the lung bases and engorgement of the lung roots seen on cardioscopy, and by a general lack of translucency (see *Plate* 26) *There may also be small collections* of fluid in either pleural cavity. At this stage the pulmonary second sound will be accentuated The patient will have orthopnœa, and may experience attacks of acute paroxysmal cardiac dyspnœa, with perhaps bronchospasm or of pulmonary œdema. In addition there are two specific signs that should be sought.

Pulsus Alternans. A weak beat alternates with a stronger. The spacing is usually regular. Occasionally th... ...val preceding the weak beat is longer th... ...s the weaker contr... ...). Premature con... ...mal beats may give a superficial rese... ...to true alternation. Here, however, the longer interval

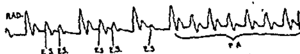


Fig 78
Alternation of the pulse following a bout of extrasystoles
P A=pulsus alternans

Sometimes a premature contraction causes alternation to appear for a few beats. Alternation may appear in paroxysmal tachycardia or in flutter. Alternation is well shown by graphic tracings of the radial pulse (Fig. 78). It may be detected by the sphygmanometer easily if the pressure in the bag is allowed to fall slowly as the beat first comes through. Records of the apex beat do not always agree with the pulse. Sometimes there is no alternation over the apex; in other cases the stronger apex thrust coincides with the weaker pulse beat. Occasionally alternation in the voltage of the R waves can be seen, in the electrocardiogram (Fig. 79).



Fig 79
Alternation in voltage of R and T waves

Alternation of the heart beat occurs firstly when an apparently healthy muscle is greatly overburdened, as in paroxysmal tachycardia, or flutter. Secondly, when the rate is not fast but the heart muscle is much diseased. It is most commonly seen in patients with high blood pressure when the myocardium is beginning to fail. It is also met with in old people, in whom there is disease of the coronary arteries, angina pectoris or cardiac asthma. Its presence would appear to indicate exhaustion of the muscle.

Nature of Alternation. In alternation all the fibres of the heart do not contract at each systole. The fibres which fail to contract may be diffused throughout the muscle, or more may fail in one

part of the muscle than in another. Lewis (81) suggested tha when the rate of the heart is high, the refractory period of some fibres may last longer than diastole, so that they are not ready to respond to every beat. Alternation at a slower rate occurs in diseased hearts, and it is possible that here, too, a gross prolongation of the refractory period takes place in some fibres, so that they cannot respond to every beat. Alternation is a sign of the gravest import: few patients live long in whom this serious indication of defective contractility persists.

Gallop Rhythm. Gallop rhythm denotes the presence of a third heart sound. This sound is usually presystolic in time, and is related to the succeeding first sound. It is low in pitch, dull, and may vary a good deal in intensity. It is best heard either just internal to the apex beat or to the left of the xiphisternum when it is right ventricular in origin. The apex beat is reduplicated. This double beat, often assuming a wavy character, is best felt with the flat of the hand applied to the chest. It is often clearly visible in a thin patient. The additional or weaker thrust precedes the true systolic thrust, and is synchronous with the gallop sound. In cases of hypertension the sounds of the heart may be described by writing $3\,\bar{1}\,2$; or $3\,1\,\bar{\bar{2}}$ when the first sound has become weak, or sometimes, when there is no hypertension, the sounds are equal in loudness, 3 1 2 The position of the sound in the heart cycle is usually presystolic, but its relation to the preceding second sound may vary with the length of diastole, which depends on the rate of the heart. This variation in the position of the sound has given rise to the terms "protodiastolic" and "mesodiastolic" to describe it. Gallop rhythm is usually associated with some tachycardia, but may be found with a rate of eighty a minute; in these cases there is often a synchronous ventricular contraction due to bundle branch block.

Causation. Sound tracings taken simultaneously with electrocardiograms show that the gallop sound occurs at the same time as the P wave of auricular systole (82). When the left ventricle is weakened and dilated, the blood entering it sets up vibrations in its wall that can be seen, felt and heard. Probably a lack of tonus of the myocardium is the underlying defect. When auricular fibrillation is present, gallop rhythm is not found. When a beat

Clinical Significance. Gallop rhythm occurs most commonly in hypertension. It is met with also after coronary occlusion, in aortic incompetence, in acute myocarditis as in diphtheria, in arteriosclerotic heart disease without hypertension and in severe anæmia. It is heard also over the right ventricle in pulmonary infarction and emphysema. It betokens ventricular failure. Often it is heard for a short time only, disappearing as the failure recedes with treatment. A persistant gallop is of serious import and has a bad prognosis.

DIFFERENTIAL DIAGNOSIS. Gallop rhythm must be distinguished from other additional heart sounds, most of which are of no importance.

The Normal Third Heart Sound. A third heart sound can often be heard in young people when they are examined in the *reclining* or left lateral position, especially if the heart rate is raised from anxiety. The sound is best heard internal to the apex: it is light and sharp in character, and of higher pitch than the gallop sound. It is due to the distension of the relaxed ventricle during the phase of rapid inflow of blood from the auricle (83). It is *never* found in subjects who are over forty years of age. It *follows* the second sound by about .19 second (81). It is met most *frequently* in those with vertical hearts and, in them, the pulmonary arc is usually prominent.

Auricular Systole. In heart block with a prolonged P-R interval, the auricular component of the first sound may be separated from it and may become audible.

A "splitting" of the first sound may be heard in healthy people. This is composed of a dull element, which may be auricular and a sharp sound which follows. It has no significance.

Bundle Branch Block. Here a true splitting of the first sound may occur from the asynchronous contraction of the ventricles. The association is inconstant. In other cases a true gallop sound may be present, or else the P-R interval may be prolonged.

Reduplication of the second sound at the base is due to the asynchronous closure of the pulmonary and aortic valves. It usually indicates increased pulmonary pressure and is therefore heard most often in mitral stenosis.

left. As this comes on, the acute distress of an overfilled pulmonary circulation is often relieved and dyspnœa is less severe. The well-known clinical paradox presents itself, in which the patient feels better but is actually worse.

Precipitating Factors

Cardiac failure has usually a gradual onset with increasing dyspnœa on effort leading to orthopnœa or to œdema of the ankles. In hypertension, nocturnal dyspnœa, with perhaps an attack of acute pulmonary œdema, may betray the presence of advanced pulmonary congestion with hydrothorax. Some attacks of pulmonary œdema are associated with over-exertion on the previous day, but in many no precipitating factor can be found. In younger patients with mitral stenosis the advent of auricular fibrillation may lead promptly to heart failure, and the same may occur in older people without valvular disease. In elderly people an attack of bronchitis may precipitate failure. The interference with oxygenation in the lungs imposes more work on the heart, and the accompanying sodium retention may lead to an increase in the blood volume

It is difficult to estimate the effects of over-exertion. Sudden death, presumably from ventricular fibrillation, may follow a sudden effort such as running for a bus. The initial phase of the subintimal hæmorrhage leading to a coronary occlusion may be caused by unusual exertion. But in the main, cardiac patients have their exertions limited by dyspnœa, and are thereby safeguarded from thus initiating heart failure.

Rhythm in Cardiac Failure. In most cases, where failure is gradual and prolonged, auricular fibrillation is present. Y...

... rhythm. A large proportion of cases of hypertension develop failure with normal rhythm.

The advent of fibrillation or flutter in any chamber marks the end of it as an effective contractile organ. V...

for a long time since the ventricles continue their co-ordinate contraction.

Commonly, the auricles give way before the ventricles, and auricular fibrillation is usually found in the terminal stages. This will apply to most forms of generalised heart disease When the auricle bears the brunt of the mechanical strain as in mitral stenosis, fibrillation will appear early

If the stress is extra-cardiac either in the systemic or in the pulmonary circulation and the heart muscle is healthy, there will be no reason why the auricles should fibrillate, and the rhythm will often remain normal. The ventricles also require more blood than the auricles, and if the coronary arteries are diseased, they may give way before the auricles have reached the stage of fibrillation These causes account for most of the cases where normal rhythm persists in cardiac failure

REFERENCES

1 GROLLMAN (1932) Cardiac Output of Man in Health and Disease
2 FORSSMAN (1929) *Klin Wschr* **8** 2085
3 COURNAND RANGES (1941) *Proc Soc exp Biol N Y* **46** 462
4 COURNAND RILEY *et al* (1945) *J clin Invest* **24** 106
5 MCMICHAEL SHARPEY SCHAFER (1944) *Brit Heart J* **6** 34
6 WARREN STEAD BRANNON (1946 Feb *Amer J Physiol* **145**, 458
7 BAZETT, LAURENCE SCOTT (1941) *Amer Heart J* **22** 737
8 STARR (1941) *Amer J med Sci* **202** 469
9 STEAD WARREN *et al* (1945) *J clin Invest* **24** 326
10 MCMICHAEL (1947) *Advances in Internal Medicine* **2** 64
11 SUAREZ FASCIOLO TAQUINI (1946) *Amer Heart J* **32** 339
12 BRANNON, MERRILL *et al* (1945) *J clin Invest* **24**, 332
13 SHARPEY-SCHAFER (1944) *Clinical Sci* **5** 125
14 EDHOLM HOWARTH MCMICHAEL (1945) *Clinical Sci*, **5** 249
15 STARR JONAS (1943) *Arch intern Med* **71** 1
16 BLOOMFIELD LAWSON *et al* (1946) *J clin Invest* **25** 639
17 WOOD MCKEE (1944) *Amer Heart J* **27** 170
18 BEDFORD, WRIGHT (1924) *Lancet* **II** 106
19 BURCH WINSOR (1943) *J Amer med Ass* **123** 91
20 WINSOR BURCH (1946) *Amer Heart J* **31** 387
21 LYONS BURWELL (1946) *Brit Heart J* **8** 33
22 ADCOCK LYONS BARNWELL (1940) *Amer Heart J* **19** 283
23 WARREN BRANNON STEAD MERRILL (1945) *J clin Invest* **24** 337
24 HOWARTH MCMICHAEL SHARPEY SCHAFER (1946) *Clin Sci* **6** 41
25 LEWIS (1930) *Brit med J* **1** 849
26 MAY (1943) *Amer Heart J* **26** 685
27 CROOK MORRIS (1942) *J Physiol* **101** 237
28 GIBSON EVANS (1937) *J clin Invest* **16** 301
29 MENEELY, KALTREIDER (1943) *J clin Invest* **22**, 521
30 NYLIN (1945) *Brit Heart J* **7**, 81
31 HILL (1941) *Lancet* **1** 177
32 KALTREIDER MENEELY (1940) *J clin Invest* **19** 627
33 WARREN STEAD (1944) *Arch intern Med* **73** 138
34 GRANT, REISCHMAN (1946) *Amer Heart J* **32** 704

35 Proger, Ginsburg, Magendantz (1942) *Amer Heart J*, 23, 555
36 Futcher, Schroeder (1942) *Amer. J med Sci*, 204, 52
37. Merrill (1946) *J. clin Invest*, 25, 389
38 Seymour, Pritchard, Longley, Hayman (1942) *J clin Invest*, 21, 229.
39 Liljestrand, Lysholm, Nylin, Zachrisson (1939) *Amer. Heart J.*, 17, 406
40 Nylin (1943) *Amer Heart J*, 25, 598.
41 [illegible]

[illegible]

31, 935.
[illegible], 215.
[illegible] 411
[illegible], 175.

[illegible] (London, 1918) The Linacre Lecture on the Law of the Heart.
57 Harrison, Cullen, Calhoun, Wilkins, Pilcher (1932). *J. clin. Invest*, 11, 133
[illegible] *Med*, 28, 121

[illegible] 5

[illegible] *Sci*, 6, 135

[illegible] 282, 293
[illegible] 423
[illegible] *Clin Sci*, 6, 187
71 Fahr (1941) *Ann. intern Med*, 5, 798
72 Reichsman, Grant (1946) *Amer Heart J*, 32 438
73 Payne, Peters (1932) *J clin Invest*, 11, 103
74 Bramkamp (1935) *J clin, Invest*, 14, 34
75 Smirk (1936) *Clin Sci.*, 2, 317
76 Abramson, Fierst, Flachs (1943) *Amer Heart J*, 25, 328.
77 Harrison, Pilcher (1930) *J clin Invest*, 8 259
78 Bedford, Lovibond (1941) *Brit. Heart J*, 3, 93
79 Altschule, Zamcheck (1944) *J. clin Invest*, 23, 325.
80 Waller, Blumgart, Volk (1940) *Arch intern Med*, 66, 1230
81 Lewis (1925) "Mechanism and Graphic Registration of the Heart Beat" 438-446
82 Lewis [illegible]
83 Tac[illegible]
84 Ev[illegible]
85 Bo[illegible]
86 Russek, Zohman (1945) *Amer Heart J*, 30 427

CHAPTER XI

TREATMENT OF CARDIAC FAILURE

The treatment of cardiac failure with congestion and œdema comprises rest in bed with suitable hypnotics to procure sleep; the use of digitalis; the promotion of diuresis by mercurial or xanthine compounds; and dietetic measures. In special circumstances venesection may be required. Other therapeutic agents include oxygen, adrenalin and vitamin B and C. Finally, in the stage of rehabilitation, massage and graduated exercise are useful.

The Digitalis Group

Digitalis is the supreme cardiac stimulant. For it and its allies, strophanthus and squill, there is no substitute.

PREPARATIONS. The active principles of digitalis are obtained from the leaves of two varieties of foxglove, digitalis purpurea and digitalis lanata. "*Digitalis Folia*" is available as "digitalis pulverata" B.P. (the dried and powdered leaf of purpurea). The lanata variety is three or four times as potent as purpurea, and from it are extracted the pure glycosides. Preparations of the leaf and the tincture vary considerably in strength, depending on the place from which the crop was gathered, and, in the case of the tincture, the age of the preparation. The preparation is standardized by finding the lethal dose for a frog or a cat from any given sample. More recently pure glycosides have been used for obtaining a rapid effect either by the intravenous or oral route. These are of known potency and are constant.

Digitalis lanata contains three glycosides: Lanatoside A, B, and C. Lanatoside A gives *digitoxin*, from which the Nativelle product of digitaline is made, and a monosaccharide. Lanatoside B gives gitoxin. Lanatoside C, the complete glycoside, is marketed under the name of *Cedilanid*. On hydrolysis this gives *Digoxin* and glucose and acetic acid.

Strophanthus is too inconstant in activity to be useful; but two glycosides of strophanthin are in use. A crystalline glycoside from strophanthus gratus is marketed under the name of Ouabain. *Strophanthin K* is an amorphous glycoside from strophanthus Kombé.

Squill has an action like digitalis but is less potent. One grain is included in the well-known Guy's pill. From the glycosides of squill, scillonin A and B, is prepared *Urginin*.

Action of Digitalis. In 1785 Withering published his account of "the use of the Foxglove" in which he says that it has "a power over the motion of the heart to a degree yet unobserved in any other medicine." Since that time much work has been done, and much written, but the manner in which digitalis acts is still uncertain.

Mackenzie thought the beneficial action of digitalis was largely confined to the slowing and steadying of the pulse in auricular fibrillation Cushny considered that the slowing of the rate was affected partly through the vagus and partly by a direct action on the muscle. In addition the strength of contraction was increased by digitalis, and the tendency to spontaneous beats by auricle and ventricle was enhanced.

The output of a normal heart is decreased by digitalis and the heart diminishes in size. The results in congestive cardiac failure are conflicting, but in many cases the output increases while the size diminishes The venous pressure falls (1)

The problem has recently been studied afresh by means of cardiac catheterization, following the administration of 1.5 mg. digoxin intravenously (2) A [illegible]
was the only constar [illegible]
the output fell, sinc [illegible]
The output also f[illegible] when the digoxin was given to patients with diseases requiring a *high* output such as anæmia or emphysema, and this applied whether the *initial* venous pressure was raised or not. In uncomplicated cardiac failure with venous congestion, the fall in venous pressure was accompanied by a rise in the output. The same effect on the output was obtained by venesection, or by occluding the venous return from the legs by means of inflated cuffs *on the* thighs. Apart from the more transitory effect of venesection, the only difference noted was that

after large venesections the arterial pressure fell slightly, whilst *after digitalis it was unaltered* or raised. The effect was the same whether the auricles were fibrillating or not. In patients with fibrillation the ventricular rate fell as is usual, but when the slowing had been abolished by atropine, the cardiac output in some cases increased still further. The conclusion was that though there was overwhelming evidence of an action by digitalis upon the veins, little evidence could be adduced by that method of any action upon the heart muscle. Apart from a small difference in arterial pressure and in the time factor, the effects of digitalis and of venesection were the same. Nevertheless, it would be premature to jettison Cushny's work altogether, and abandon what is to most a strong impression of improved efficiency. Clinical experience follows Cushny and suggests that a stronger beat results.

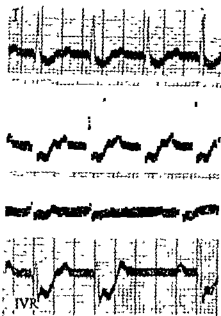


Fig 80
Digitalis intoxication. There is heart block and depression of S-T interval in all leads, especially IV R

Digitalis and the Metabolism of Potassium. Analysis of the ventricular muscle of cats who had been given digitalis to the point of causing electrocardiographic changes showed an increase in the potassium content compared with controls (3). The serum potassium was also increased in normal subjects after injections of mecholyl (4). It may be that digitalis and mecholyl are synergic, and that digitalis makes the heart muscle more sensitive to acetyl choline. This might account for the vagal action of digitalis.

Effects of Digitalis Saturation and Overdosage upon the Electrocardiogram

That digitalis has some action upon the ventricular muscle is shown by the electrocardiographic changes. They fall into three

groups; the T wave changes of digitalis saturation; the effect of intoxication upon auriculo-ventricular conduction; the increased excitability of the muscle, shown by premature ventricular systoles, and at a later stage of poisoning by ventricular tachycardia.

T Wave Changes. The earliest changes are a depression of the S-T junction and a depression of the S-T interval. This depression is concave, the opposite of the convex bowing seen in infarction. The T wave itself is diphasic or inverted. There is usually some shortening of the Q-T time (5). These changes may appear within two hours of an intravenous injection. In patients who have been digitalised they can sometimes be brought on by exercise (6). If pronounced, the T wave changes are seen in all three standard



FIG. 81
Auricular fibrillation Note inversion of T waves in leads II and III.

leads, and in all the chest leads The depression of the S-T junction in V4 and V5 is always more deep in the standard *leads* (Fig. 60); the changes may simulate a lateral infarct closely, making it impossible to diagnose that condition if digitalis has been given during the preceding fortnight. When the changes are less pronounced, the inversion of T is usually seen best in leads I and II, when the heart is horizontal, and in leads II and III when the heart is vertical (Fig. 81) This is probably due to the fact that, when the heart is vertical, the left leg lead (VF), which predominates in lead III, reflects the changes of potential over the left ventricle; whilst the left arm lead (VL), which predominates in lead I, does so when the heart is horizontal.

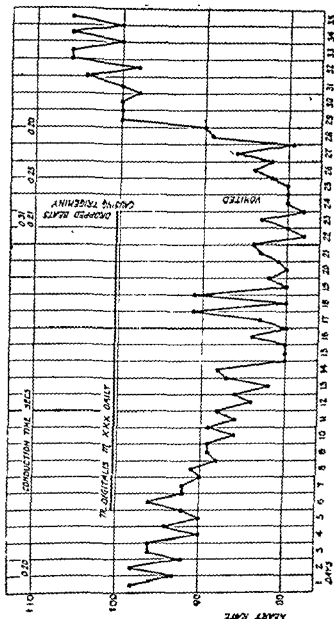


Fig 82

Digitalis medication causes vagal slowing and finally heart block, in a child of thirteen years

A-V Heart Block. Some prolongation of the P-R interval is not uncommon in digitalis saturation (Fig. 80). In digitalis poisoning dropped beats may occur, or even complete heart block. These effects are probably produced by the vagus.

In massive overdosage there is usually A-V dissociation as in the case of a woman who consumed 300 grains of the folia. She had incessant vomiting, became stuporous and died in 12 hours from respiratory failure. The auricular rate was 120, and the ventricular rate was 66 (7).

PREMATURE SYSTOLES AND VENTRICULAR TACHYCARDIA. An early sign of intoxication is the appearance of ventricular premature contractions, causing a bigeminal pulse, though coupling may be due to other causes (p. 267) The premature contractions are closely linked to the preceding normal beat, occurring on that part of the cycle occupied by the U-wave. It has been suggested that these represent a form of re-entry (see p 268) Ventricular tachycardia may occur in more serious overdosage, or when conditions favour its development as after infarction. The bi-directional type is particularly dangerous, and sudden death is likely to occur if the drug is not stopped at once (Fig. 75). Digitalis purpurea seems more prone to cause it than digitalis lanata (8)

These changes show that digitalis in full doses or in overdosage affects the myocardium profoundly. The question as to whether in therapeutic doses the drug stimulates contraction or whether its power is limited to the relief of venous congestion, presumably by relaxing the veins, must be regarded at present as unsettled. We are inclined to think that in therapeutic doses it does stimulate the myocardium in systole.

METHODS OF ADMINISTRATION. Digitalis can be given by the mouth or by intravenous injection The older method of calculating the dose required from the body weight and then administering a very large initial dose orally has been superseded.

Intravenous administration. With the intravenous preparations now available an effect can be obtained in thirty minutes, and there is less risk of severe intoxication since the effect of the intravenous dose passes off in about six hours. Full intravenous doses of digitalis should not be used if the patient has received any digitalis during the preceding fortnight.

The intravenous preparations of digitalis include digoxin, and lanatoside C (cedilanid) Strophanthin in the form of ouabain or strophanthin K are also used

Digoxin. The intravenous digital...

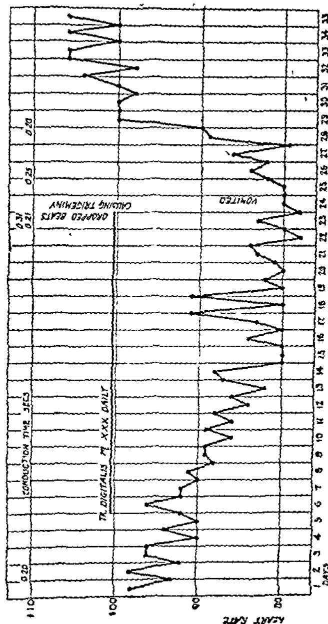


Fig 82

Digitalis medication causes vagal slowing and finally heart block, in a child of thirteen years.

A-V Heart Block. Some prolongation of the P-R interval is not uncommon in digitalis saturation (Fig. 80). In digitalis poisoning dropped beats may occur, or even complete heart block. These effects are probably produced by the vagus.

the time of the injection and to repeat the dose six-hourly until the effect is completed.

Oral Administration. If a rapid effect is not desired, digitalis can be given by mouth. Although many preparations are available, none has any advantage over the leaf (15), (16). Owing to the slower action by mouth, the drug should not be given at more frequent intervals than six hours. It is usual to give a loading dose, so that four grains of the folia might be given at once, followed by one grain six-hourly. This should lead to a full effect in about six days. The dosage may be graded according to the weight of the patient. With those over twelve stone, 1½ to 2 grs. may be given six-hourly. Single large doses have been given to patients with fibrillation in order to ascertain how long the action continues. After 13 grains of the folia the rate did not return to the former level for an average of eighteen days; after an equivalent dose of the Nativelle digitaline the interval was eleven days (17). It seems that the pure glycosides are eliminated more quickly, so larger maintenance doses are required (18).

Maintenance Digitalis, once begun, has often to be *continued indefinitely*, but a smaller dose is required to maintain the correct concentration. About one grain is eliminated daily, so that maintenance doses vary from gr. 1½ daily in small people to gr. 4½. Most patients take two or three grains. These doses may be on the low side. In one series of 100 cases who were admitted in congestive failure while on maintenance doses, 4 cc. of cedilanid (0.8 mg.) which is half the full dose, was given intravenously (19). Three-quarters improved. The treatment was not given to any who had a ventricular rate below ninety when fibrillating. No toxic reactions were observed in this group but six reactions occurred in those with normal rhythm. We have found this method successful and free from risk. In a comparison of the three glycosides given orally for maintenance, digoxin was found to be more satisfactory than digitaline or lanatoside C. (Cedilanid). Occasionally a patient cannot tolerate the folia on account of vomiting, and the glycoside may then be used. Digoxin was found to be better than digitaline or lanatoside C for this purpose (20).

Squill. In other cases a good result in these circumstances may be obtained by using urginin (21), a preparation of squill, 0.5 mg. tablets of which are approximately equal to gr. 1 of digitalis folia

2 to 3 ampoules The dose may be diluted with 10 cc. of saline, but is quite safe if given very slowly without.

Cedilanid is supplied in 2 cc. ampoules containing 0.4 mg. each. The average intravenous dose is 4 ampoules or 1.6 mg. No dilution is necessary.

Ouabain ampoules contain 0.25 mg. The average dose is 0.5 mg.

Strophanthin K is given in doses of 0.25 mg. dissolved in 10 cc. saline (9).

An equivalent dose of cedilanid, digoxin, ouabain, and digitoxin (Nativelle digitaline) was given alternately to one patient at intervals of a few days (10). With the first three the effect began within ten minutes ouabain being the quickest and then digoxin. The venous pressure and the pulse rate fell to normal. Cheyne-Stokes respiration was abolished in thirty minutes In another comparison the venous pressure began to fall from three to ten minutes after ouabain and in from five to twenty minutes after digoxin (11)

Cedilanid in doses of 8 cc. (1.6 mg.) produced nausea only in three out of 40 cases (12) The drug is excreted rapidly so that any symptoms of overdosage do not last long. After digoxin in doses of 1.5 to 2 mg. two patients died, one suddenly and one from ventricular tachycardia (13)

To maintain the effect after intravenous digitalis it is necessary to give digitalis folia by mouth at the same time Two grains should be given with the injection, and that dosage is continued at six hourly intervals until there is full saturation with digitalis. In one series the folia was given in one dose at the same time as the injection (14) The dosage was 6 grains for those under nine stone 9 grains for those up to twelve and a half stone, and 12 grains for those above There does not seem to be much advantage to be gained from the single dose, since patients vary greatly in the amount of digitalis they require apart from their weight

Summary. Several reliable intravenous preparations are available by which an effect can be obtained in less than thirty minutes. Of these ouabain appears to act the quickest, with digoxin second. Of the two, digoxin is preferable. With cedilanid the margin between the effective and the toxic dose is probably the greatest. Since the effect of an intravenous dose does not last long it is best to give digitalis orally in doses of two grains of the folia at

without failure treated with lanatoside C given orally, 90 per cent showed an increase in the stroke output after a week (25).

Auricular Fibrillation and Flutter. The action of digitalis in these arrhythmias is discussed in Chapter IX. Digitalis is also indicated in paroxysmal auricular tachycardia in children (see p. 300) and in auricular tachycardia with A-V heart block (see p. 287)

CONTRA-INDICATIONS TO DIGITALIS. Digitalis should be avoided in cardiac infarction owing to the risk of ventricular tachycardia.

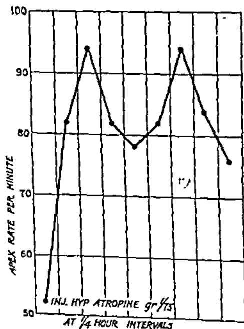


FIG 83
Chart of apex rate in auricular fibrillation, showing abolition of digitalis slowing by atropine

The ventricular muscle after infarction is irritable, and more prone to ectopic rhythms than usual.

When there is impairment of conductivity of the bundle of His, the administration of digitalis will enhance this defect. Delay in the passage of the impulse may be increased to complete heart block; moderate doses should be employed. Dropped beats contra-indicate digitalis. Digitalis may be given in full therapeutic

Digitalis Intoxication. As has been mentioned, heart block, premature systoles, and ventricular tachycardia may all result from overdosage with digitalis. Sudden death is probably due to ventricular fibrillation. Accompanying these are anorexia, nausea, vomiting, headache, diarrhœa and green or yellow vision. A diminution in the excretion of urine also occurs. The earliest signs which should be watched for are anorexia and the coupled rhythm due to premature ventricular systoles. When these appear digitalis should be stopped for twenty-four hours and maintenance doses then substituted.

Digitalis poisoning may come unexpectedly in the following way. If full doses have been employed, and particularly if a mercurial diuretic has been given at the same time, a massive diuresis may take place. The fluid is lost from the body cavities, and from the tissues generally, with an accompanying fall in the blood volume; but the digitalis is left behind. The concentration of the drug may then increase to the point at which signs of intoxication occur. All that is needed is to omit the digitalis for a day or so until the balance has been restored.

For serious overdosage the most effective remedy is atropine which should be given, intravenously if necessary, in doses of gr. 1/30 to 1/50 (Fig. 83).

Indications. *Cardiac Failure with Venous Congestion* is the main indication for digitalis. It does not matter if the auricles are fibrillating or the rhythm is normal (22); the results should both be good. Only if the venous congestion has been allowed to progress too far will a venesection be necessary before digitalis can succeed. With auricular fibrillation the dosage is easier to control as the rate will fall and the dose can be continued until the apex rate has reached a level of 80. In patients with normal rhythm, tachycardia is often not affected by digitalis (23), and it is necessary to be guided by diuresis, if there is œdema, or to continue till early signs of intoxication appear. In children with rheumatic carditis, digitalis often slows the tachycardia as the saturation point approaches (Fig. 82). Patients with left ventricular failure secondary to hypertension usually respond very well, even if the systemic venous pressure is normal (24). Those with cardiac enlargement and dyspnœa benefit from moderate doses such as Guy's pill once or twice a day. In one series of cases

fibrillating, may need larger doses than ordinary. Sedatives are a useful help here. Digitalis is less effective in the presence of fever, and has no influence on the associated tachycardia. The rapid ventricular rate due to auricular fibrillation can be controlled in fever, but abnormally large doses will be needed.

Promotion of Diuresis

There are several means of promoting diuresis. Digitalis alone, by improving the circulation, may cause œdema to disappear. Guy's pill, containing a grain each of digitalis leaf, mercury and squill, is often efficacious If the œdema is extensive, it is best to employ diuretic drugs in addition to digitalis. These comprise the mercurial diuretics and xanthine group. A diet low in sodium also helps. Should the œdema resist these measures, special collections of fluid may have to be [illegible] removal of œder [illegible]

Xanthine De [illegible]

an isomer of theobromine. It is closely related to caffeine. Cardophylin or amino-phylline, is theophylline-ethylene-diamine, and is by far the most potent member of the group.

Cardophylin is supplied in ampoules of 2 cc. containing .48 g. for intramuscular use, and of 10 cc. containing .24 g. for intravenous injection. We have found it quite safe, and more convenient, to use the intramuscular ampoule of 2 cc. intravenously, giving 1 cc slowly as a rule, but 2 cc. if a full effect is desired.

The action of cardophylin, apart from that of a diuretic, has been studied with the auricular catheter (26). An intravenous injection of 0 48 g. was given to normal subjects, and to those with various types of heart disease In every case the right auricular pressure fell in about five minutes. In hypertensive heart failure a striking rise in the output occurred and lasted up to thirty minutes. In mitral stenosis with auricular fibrillation the rise was moderate. In normal subjects, and in those with emphysema, a transient rise in the cardiac output occurred, but this fell soon below the initial level as the effect [illegible]

[illegible] rapidly and [illegible] considerable rise in the output was observed with [illegible]

doses to patients with complete heart block. Stokes-Adams attacks will not be produced. *There is no effect, as a rule, on the ventricular rate, but the systolic contraction is improved.*

Bundle branch block is no drawback. Indeed, a bundle branch block may disappear on occasion as the circulation improves (Fig. 84). *Pulsus alternans* does not forbid it. The presence of premature contractions, apart from those due to the exhibition of the drug, does not matter. Vomiting from heart failure is a call for digitalis, and will cease when the beneficial effect of the drug has been achieved. When a patient with heart failure due to the tachycardia of auricular fibrillation vomits, the administration of digitalis is urgently needed.



FIG. 84

Auricular fibrillation and left bundle branch block. Lower strip: Forty minutes after cedilanid. The *QRS is normal apart from the first complex.*

CASES WHO FAIL TO RESPOND. Patients who require a high output to maintain the circulation on account of anæmia, or chronic disease of the lung, may not respond to digitalis, even though the venous pressure is high (25). The venous pressure falls but so does the cardiac output. Some cases of chronic lung disease respond well, however, and digitalis may be worth a trial. For anæmia there are other remedies. Cases with aortic valvular disease often do badly, especially when the lesion is due to syphilis. The presence of chronic renal disease is an unfavourable complication. The sinus tachycardia of hyperthyroidism is not controlled by digitalis, and in these patients the tachycardia due to auricular fibrillation often needs abnormally large doses to reduce it. Nervous patients, with strong sympathetic tone, when

includes a phenol ring and is supplied in 2 cc. ampoules, containing 0.84 per cent of active substance for intramuscular injection, and in ampoules of 10 cc. containing the same quantity for intravenous use. Both mersalyl and neptal now include also theophylline in the proportion of two parts of mercury compound to one of theophylline. Thus the combined effect of mercury and theophylline is obtained. Tablets of neptal containing 0.18 g. are also available for oral use. Suppositories were formerly obtainable, but they proved to be irritating and they are not now used.

ACTION. The exact mode of action of the mercurial group is uncertain but they cause the kidneys to excrete more sodium and diuresis follows. The action is enhanced by acidifying drugs such as ammonium chloride or ammonium nitrate taken by the mouth. The diuresis begins rapidly, often within thirty minutes of an intravenous injection, and it may be over in twelve hours, although frequently it continues on the following day. It is usual to give the injection early in the morning so that the patient is not disturbed during the night. The addition of theophylline enhances the effect, and lessens the risk of mercurialism since the drug is excreted faster.

TOXIC REACTIONS. *Mercurialism.* In susceptible people stomatitis, or hæmorrhagic colitis may occur Cramp may be caused through loss of serum chlorides (27) These reactions with modern preparations are rare Erythematous or morbilliform rashes accompanied by itching are occasionally seen. For these a patch test is useful (28) Lint soaked in the intramuscular solution of neptal is applied to the skin. A positive reaction is shown by irritation within 24 hours, and indicates accumulation of the drug in the tissues from excessive dosage, poor diuresis, or renal impairment. After a period of rest the test may become negative and injections may be resumed.

Renal Changes. Hæmaturia or anuria may be caused in patients with nephritis, and death may ensue from uræmia. Mercurial drugs should not be given to such patients

Sudden Death. Cases have been recorded of sudden death after an intravenous injection. The patient collapses and becomes unconscious There may be convulsions, and death takes place in a few minutes. Most of the deaths have occurred in patients with nephritis or nephrosis; the others show a fairly consistent sequence of events. The patient has received a course of intravenous injec-

During the course of injections the urinary output is measured daily. Sometimes as much as 300 ozs. may be passed in the forty-eight hours after an injection. The course is continued until all the œdema has gone, and the daily output has fallen to the neighbourhood of 40 ozs. It is helpful to take also the weight of the patient before and a day after the injection. If the fall is not more than 3 lbs. the œdema has probably cleared. It has been suggested that the course should be continued until the daily range of the change of weight does not exceed 5 lbs. for a fortnight. Ammonium chloride is then continued in doses of 2 g. three times daily, and the mercurial injection is recommenced if the weight rises. By this method it is claimed that all œdema is removed (34)

By Mouth. Tablets of neptal are useful when œdema tends to recur early. Three tablets should be taken once or twice a week, preceded by a single dose of thirty grains of ammonium chloride.

Tablets have been given daily for periods up to sixteen months, (35). The dosage varied from 2 to 6 tablets with average of 4. One or two grammes of ammonium chloride or ammonium nitrate were usually taken three times a day at the same time. Satisfactory diuresis was obtained in most cases though it did not begin for about a week (36). Toxic effects occurred in half those treated over long periods consisting of vomiting, diarrhœa and abdominal pain. Uræmia occurred twice, and this method should not be used where there is impairment of renal function.

Indications. When the patient has much œdema, digitalis should be given at once and intravenous neptal preceded by ammonium chloride on the following morning. It is not always appreciated that pulmonary congestion responds as well to neptal as does peripheral œdema. Patients with left ventricular failure with orthopnœa and nocturnal dyspnœa may expect to have a considerable diuresis and great alleviation of symptoms. Lastly, there are a few conditions such as coronary occlusion where digitalis is inadvisable. If pulmonary congestion develops, neptal is the most effective remedy available.

Contra-Indications. The only important contra-indication is nephritis. It is our practice not to give neptal if the blood urea exceeds 60 mg. In doubtful cases we prefer to wait until the test has been done, using cardophylin in the meantime If the drug

tions and the last few have given rise to apprehension, or transient dyspnœa, or pain in the chest immediately after the injection. The course is continued, and the next injection causes sudden death (29). The cause of death is probably ventricular fibrillation through a direct action the mercury ion upon the ventricular muscle (30). Fatalities seem to occur especially in patients with chronic wasting disease and old-standing œdema. No death has been recorded after an intramuscular injection. It is claimed that the 10 cc. ampoule, being more dilute, will be less likely to cause unpleasant reactions. Out of the many thousand injections that have been given the number of fatalities has been extremely small (22 only had been recorded, including those in nephrosis, up to 1942) (31). Provided that watch is kept for transient symptoms of apprehension or dyspnœa, and that patients with renal lesions are excluded, *intravenous injections are quite safe. We have had one* death in nephrosis, but no unpleasant reactions in cardiac cases, though occasionally intravenous injections have been discontinued owing to the warning symptoms.

Administration. *By Injection.* Intravenous injections are about one-sixth more efficient than intramuscular (32). The intravenous route is painless apart from the puncture, though necrosis may result if the solution escapes from the vein. Intramuscular injections are apt to cause a sharp stinging pain for about fifteen minutes after the injection. Unless they are given carefully they may lead to abscess formation or even to sloughing of the skin. An œdematous area should be avoided. With either route the effect is enhanced by preliminary administration of ammonium chloride or nitrate. These drugs are nauseating, but can be taken in enteric coated capsules of 7½ gr. each. Formerly 1-2 g. were given three times daily, but it was found that an equally good diuresis resulted when one dose of 2 g. (4 capsules) was taken two hours before the injection (32). To avoid mercurialism, injections are not given more frequently than every third day, except in urgent cases when they may be given every other day for a limited time. One may give ammon. chlor. gr. xxx early in the morning, and intravenous neptal 2 cc. two hours later. Good results have been claimed from intravenous cardophylin given one hour before the intramuscular injection of mersalyl (33) but we have not found that this offers any special advantage.

The diet involves washing the butter to free it from salt: salt free bread is also needed. Altogether it imposes a considerable strain upon the dietitians. Specimen sheets are appended, but we doubt if the method will have any general application in this country until the food situation eases. Nevertheless there are patients who improve dramatically; and the relief from the restriction of fluid intake is much appreciated.

Acid Ash Salt Poor Diet (from Schemm).

A. Unrestricted foods (from which at least two or three servings should be taken for any one meal).

Eggs.—Two may be substituted for one meat serving.

Meats.—Any fresh meat, fish, or chicken, one serving daily.

Bread.—Whole wheat bread without salt or raisins.

Cereal.—Puffed rice, puffed wheat, shredded wheat or any hot cereal cooked without salt.

Macaroni, spaghetti, rice cooked and served without salt or sauce.

Fruit.—Prunes, plums, cranberries.

B. Restricted foods (from which no more than two servings should be taken at any meal).

Vegetables.—Two small servings daily of any vegetable except parsnips, beans, rhubarb, chard and spinach, which are forbidden; use fresh or frozen vegetables or those tinned without salt.

Fruit.—One serving of fruit or fruit juice daily except raisins and dates, which are forbidden.

Milk and Milk Products.—Two cups milk daily, one-quarter cup cream daily; unsalted cottage cheese substituted for meat.

C. Soup.—May combine allowed vegetables with milk allowance or with salt free broth.

Sweets.—Plain jelly or pudding made from allowed eggs, milk, bread, cornflour, junket (no cakes or pastry).

Beverages.—One cup of coffee or tea at each meal.

Neutral foods (which *may* be taken in any quantity):—

Sugar, butter, salad oil, clear sugar candies.

is not given more often than at three day intervals, mercurialism is extremely rare. Should a patient develop transient symptoms immediately after an injection, such as apprehension or dyspnœa, the intramuscular route should be substituted for the intravenous.

Low Salt Diet. Since the increased blood volume which leads to œdema is due to the retention of sodium in the body, a diet low in salt should aid materially in the removal of œdema. It has been the practice for many years to stop salt as well as to restrict fluids to about 20 ozs daily when œdema is present. Recently it has been shown that an ordinary diet with no added salt taken contains about 4 g. of salt daily. If no salt is used in the cooking, the salt is reduced to about 2½ g By using special diets which aim at securing a neutral or acid ash, and avoiding all medicines containing sodium, the intake of salt can be further reduced to 1 g. or less, and at this level restriction of fluid is unnecessary, since the patient will excrete all he drinks (37). If desired, fluids can be forced up to 7,000 cc. daily though this is probably unnecessary Ammonium chloride 1 g. six hourly (since the ammonia forms urea and the chloride combines with the sodium), and dilute hydrochloric acid ♏ v hourly during the day may be given at the same time (38).

When a diet containing 2 5 g. of salt, with 9 g of ammonium chloride daily was given to normal subjects they lost an average of 3 kilogrammes each in four days and the volume of the plasma fell by 430 cc (39). The serum protein also rose. In a series of patients with cardiac œdema 1 75 g. of salt, which equals 0 7 g of sodium, was given and water was unrestricted. Half the patients were substantially improved (40) In another series the patients received 2 g. of salt and in rotation restricted fluids unrestricted fluids, and forced fluids up to 7,500 cc (41) The first group were uncomfortable and tended to become dehydrated in hot weather. In the second the consumption varied from 1,300 to 2,700 cc. depending on the weather. Many patients in the third group became nauseated, but some improved greatly especially those with chronic nephritis and hypertension. The conclusion was that with such a diet patients should be allowed to drink as much as they wish, and for this many are duly grateful. The clinical paradox of thirst and a dry tongue in a patient waterlogged below the waist is thus avoided

a high venous pressure. Oxygen will relieve the heart from the extra work involved in producing the faster circulation needed to overcome cyanosis, and also relieves myocardial anoxæmia. A combination of these remedies is required in emergencies such as cardiac asthma and pulmonary œdema. Adrenalin has a special, though limited, place in the treatment of cardiac asystole.

Rest

The patient must be confined absolutely to bed under the care of a competent nurse. All unnecessary movements must be avoided The type of bed designed by Lewis (42) is very useful for cardiac cases, as it can be altered to provide the most comfortable angle at which the patient finds that he can recline. In addition to physical rest, sleep and mental repose are essential. Restlessness, anxiety, and dyspnœa, with cough, are the chief enemies to sleep. The voluntary movements of dyspnœa, which are substituted for the unconscious acts of normal breathing, are disturbing. Ventilation may well be diminished without harm if the reflexes provoking it are quieted. A less than normal oxygen saturation can quite well be tolerated The arrangement of pillows is important, as slipping down in the bed during sleep may provoke attacks of cardiac asthma.

Morphia. Morphia is the most valuable drug in the acute stages of heart failure. In an uncomplicated case of heart failure the effect is entirely beneficial (Fig. 86). Morphia is dangerous in heart failure secondary to kyphoscoliosis (43), also when the failure is complicated by sepsis. Old people are sometimes very sensitive to morphia. Otherwise it is free from all risk, and much harm may be done by withholding it. In emergency gr. 1/6 should

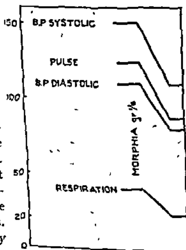


Fig 86

Chart showing the effect of morphia on the pulse, respiration, and blood pressure at the end of half-an-hour, in an attack of cardiac asthma

Dietary Precautions.

1. No salt substitutes or soda to be used in cooking or at table. Potassium chloride may be taken instead.

2. Obtain sweet butter or wash butter to remove salt; buy or bake unsalted bread or use Matzuths

3. No tinned meat or fish; no cheese except cream cheese.

4. For gas or indigestion, use no sodium bicarbonate, alkali powders, or tablets except calcium carbonate, avoid the cabbage family, turnips, peppers, radishes, onions, spices, fried foods.

5. For extra liquids use only well diluted plum, prune, or cranberry juice

Mechanical Drainage. *Paracentesis is usually the last resort, but it should not be delayed too long*

Fluid may accumulate in the legs, in the abdomen, or in the pleural cavities. Although the dropsy usually spreads upwards from the dependent parts, in special circumstances large collections may form in the abdomen as in Pick's disease, or in the chest. The legs may be drained by multiple punctures or Southey's tubes. In order to obtain the maximum effect the patient should be sitting up for twelve hours beforehand. Ordinary precautions against sepsis must be taken, but in these patients the punctures are much less likely to become septic than those suffering from renal disease. Paracentesis of the abdomen or chest will not often have to be performed It may be necessary to tap a special accumulation in the abdomen if it is causing serious embarrassment to breathing Before doing so the foot of the bed should be raised. The kidneys may function better when it has been removed. A large hydrothorax should always be removed early.

The removal of fluid from any of these parts may promote a diuresis which will take away the rest of the œdema.

Treatment of Acute Heart Failure and of Cardiac Emergencies

In the acute stage of heart failure the aim of treatment is to relieve the labouring heart of as much of its load as possible. In addition to the improvement in the circulation effected by digitalis and diuretic drugs, much can be done by providing physical and mental rest. Venesection may be needed to lower

ligature is needed. A large-bore transfusion needle may be used. Some prefer to attach the needle to an aspirating bottle. The needle is more painful than a knife, unless the skin is first anæsthetized. On the whole, we prefer the knife, which can be used quite neatly and cleanly with a little practice.

RESULTS. Apart from those patients who are snatched from death, a successful venesection always causes great symptomatic relief. The right auricular and venous pressures and the arterial blood pressures fall; the output rises (see p. 311). The effects do not last long but can be maintained by the use of digitalis after the venesection. Exceptions to the generally good results of venesection are found in those conditions in which a raised venous pressure is needed to maintain the output. In some cases of chronic pulmonary disease with a low blood pressure the output fell with the venous pressure and the patients were not improved (44).

APPLICATION OF LEECHES. Only a little blood can be removed by this means: they are no substitute for venesection. But sometimes striking relief is afforded to a patient with an enlarged and tender liver by putting six leeches along the right coastal margin. The enlargement of the liver seems to melt away and the patient will return again for a repetition of the treatment.

Oxygen

Although arterial oxygen deficiency does not occur in uncomplicated cardiac failure, oxygen unsaturation is a feature of heart failure secondary to chronic pulmonary disease. Cyanosis is also prominent when there is much pulmonary congestion. In both these conditions oxygen may bring relief; indeed in the first it is almost the only remedy available.

Administration of Oxygen. The most effective way of giving oxygen is by means of a tent, in which the patient breathes 40-50 per cent pure oxygen. We have found the open-top type, in which the patient is not cut off from sound, to be the most useful for cardiac cases. The tent can be employed for two or three days and then discontinued for short periods at first to note if cyanosis returns. If a tent is not available, a B.L.B. mask can be used for long periods, if given for fifteen minutes each hour and continued until cyanosis disappears. Six litres a minute raises the

be given intravenously, and gr. ¼ at the same time subcutaneously. Otherwise gr. ¼ should be given subcutaneously on the first evening, preceded by fifteen minutes by atropine gr. 1/50 if the lungs are much congested. The dose may be repeated on the second night, if needed, but further administration is undesirable owing to the constipating effect on the bowels.

Hypnotics other than Morphia. In chronic heart failure hypnotics may be needed over long periods. Heroin gr. 1/6 to gr. 1/12 may be placed under the tongue. It is particularly useful for the non-productive cough of pericarditis or that due to pressure on the bronchi from enlargement of the left auricle. A linctus containing heroin (gr. 1/6) or codeine (gr. 1/4) is effective.

Paraldehyde is often well tolerated, but may cause nausea. It is best given in brandy or creme de menthe. *Bromide* (grs. 30) may alone do all that is needed. It works well reinforced by chloral (grs. 15). *Nepenthe* ♏ xx may be added. The *barbitone* groups are most useful when insomnia has to be defeated or when there is nervous unrest. They are less effective if dyspnœa or pain is present. Phenobarbitone, dial, medinal (soluble barbitone) are the best of the large number available

Venesection

The question of the need for bleeding should always be considered when a case of acute heart failure is first seen. Nothing affords quicker relief in a suitable case. The indications are to be sought in the external jugular veins. When these stand out tense, blood should be let. It has been shown that when the venous pressure is very high, the pressure in the right auricle may even be higher still during part of the cardiac cycle, causing the column of blood to move backwards and forwards (see p. 313). In these circumstances digitalis is useless, and nothing but a substantial venesection will save the patient from imminent death.

Method. The essence of bleeding is the sudden removal of a large quantity of blood from one of the veins at the elbow. The amount will vary from 12 to 20 ozs. The old-fashioned method of opening the cephalic vein longitudinally by a small cut with a sharp lancet or tenotomy knife is as good as any. Raising the arm, and applying light pressure, will soon stop the bleeding. No

DIET SHEET 1

About 1,500 Calories.

Time	Fluid	Ozs	Protein	Ozs	Carbo-hydrate	Ozs	Fat	Oz.
a m 8 9	Milk Weak tea Coffee	5	Beaten egg 1		Toast Preserve Sugar	1 ¼ ¼	Butter	¼
1 30	Milk	5			Jelly	2		
p m 1 30	Orange juice	5	Fish or chicken	2	Toast Sweet Glucose	1 1 1	Butter	¼
4 30	Weak tea	5			Biscuit or toast Sugar Preserve	1 ¼ ¼	Butter	¼
7.30	Milk	5	Beaten egg	1				

The fluid may be increased if the sodium intake is kept low.

DIET SHEET 2

About 2,500 Calories

Time	Fluid	Ozs	Protein	Ozs	Carbo-hydrate	Ozs	Fat	Oz.
a m. 8 9	Weak tea Coffee	8	Egg 1 Bacon	1	Toast Preserve	2 ¼	Butter	¼
11 30	Milk	5			Biscuit	1		
p m 1.30	Orange juice whiskey and water	10	Chicken or Fish or Boiled meat	3	Mashed potato Toast Pudding or fresh fruit Glucose	2 1 2 1	Butter	¼
4 30	Weak tea	8			Biscuits Sponge cake Toast Preserve Sugar	2 ¼ ¼	Butter	¼
7.30	Orange juice, whiskey and water	8	Egg 1		Bread Pudding Glucose	1 4 1	Butter	¼

alveolar O_2 to 60 per cent. The nasal catheter method is rather wasteful of oxygen but can be quite effective, raising the alveolar O_2 to 27 per cent from the normal of 14 per cent, when the flow is at three litres a minute.

Treatment of Cardiac Asthma and Pulmonary Œdema

In cardiac asthma intravenous cardophylin by stimulating the heart and relaxing the bronchospasm may terminate the attack quickly. Intravenous morphia should be given as well to control the anxiety of the patient. If pulmonary œdema supervenes, a venesection is needed, followed by intravenous digitalis, the dose depending upon the amount of the drug that has been taken previously.

ADRENALIN. *Adrenalin stimulates the sympathetic nervous system and constricts the arterioles throughout the body, so causing the blood pressure to rise. It is also a cardiac stimulant. Subcutaneous injection leads to a great increase in the output as well as to acceleration of the beat. In larger doses, and when given intravenously, adrenalin stimulates powerfully that function of the heart muscle which is called irritability. Multi-focal ventricular premature systoles are produced and ventricular tachycardia or fibrillation can easily follow. It is this action of adrenalin which underlies its main clinical use. For adrenalin is strikingly successful in initiating a ventricular premature beat which may terminate a Stokes-Adams attack (Fig. 47). It is also employed by intracardiac injection in cardiac asystole during anæsthesia, and in vagal bradycardia causing faintness.*

In the treatment of cardiac failure, adrenalin has no place since it raises the blood pressure. This would increase the load upon the heart, and outweigh any good than might be expected from the temporary stimulation, or from the relief of bronchospasm.

Diet

Apart from the low salt diet for use in œdema, certain principles regarding the diet in heart failure need to be considered.

In severe heart failure nausea and vomiting are liable to be troublesome and the appetite is poor. As a result the protein intake may be too low and the plasma proteins reduced. Meals

Reduction of the Basal Metabolic Rate

In many cases of heart failure the B.M R. is raised (p. 325). It was natural that efforts should be made to reduce it in the hope that benefit might accrue to the failing heart. Total thyroidectomy was performed but the method has not proved a success. The patients became myxœdematous, but they were more miserable in their myxœdematous state than they had been previously with the symptoms of failure. Recently an attempt has been made to reach the same result with methyl thiouracil, the average dose being 0.2 g. thrice daily (45). Some success was noted in patients with high output failure due to emphysema. In them the outlook is so bad that any form of treatment is legitimate. But thiouracil has certain dangers, and the treatment requires constant supervision. In most cases of heart failure a normal thyroid is best left alone.

Massage and After-Treatment

The aim of the after-treatment of cardiac failure is to shorten the period of convalescence, and to put the heart in the best state subsequently to maintain the circulation for as long a time as possible. This can be accomplished by massage, and by a careful rearrangement of the life of the patient.

Rest in bed should be continued until there is no longer any venous engorgement, œdema or congestion in the lungs. Further progress may be gauged by the cardiac rate. Not until the rate of the heart has been constantly under 80 for some days may the patient be allowed to get up.

Massage. Massage may often be usefully employed in the earlier stages to assist in the removal of dropsy. The œdema fluid is stagnant and the tissues are incapable of reabsorbing it. Massage of the lower extremities, with kneading of the muscles, will help the venous return, and force the fluid to circulate. A diuresis will be promoted, the nutrition of the tissues will be improved, and the body as a whole will benefit.

The chief use of massage is in the stage of convalescence. Muscles that have become limp and weak after a long confinement to bed are badly fitted to support the weight of the body. This imposes a greatly increased load upon the heart muscle when walking is first attempted. Massage (effleurage and kneading) t

increase the work of the heart as the output is raised during digestion. Dyspepsia disturbs the heart by leading to ærophagia. Gastric distension, or distension of the colon through fermentation, interferes with the action of the heart mechanically.

In the most acute type of failure, such as after a large infarct, nothing can be tolerated for the first day or two, expect glucose drinks. But as soon as possible a light, easily digested but nutritious diet should be substituted. Meals should be small and spaced evenly through the day. It is important to tempt the patient's appetite rather than to follow any rigid programme too closely.

Two schemes for diet are suggested. One light, for severe failure, and the other heavier, for less severe cases. Modification is possible to suit individual cases in many points.

Starchy food should be reduced if gastric flatulence is prominent. Toast should be made from stale bread.

ALCOHOL. Champagne stimulates appetite, and in small doses is good for nausea. Alcohol, as brandy or whiskey, is useful in small repeated doses in the acute phases of failure, if the patient takes it. It is a useful stimulant, and promotes a sense of well-being.

TOBACCO. Patients with heart failure are better without smoking. The inhalation of tobacco smoke is very likely to set up troublesome coughing. The inveterate smoker, who finds it hard to give up tobacco, is particularly prone to this. Patients with angina who have been heavy smokers are better without tobacco. But a few cigarettes a day, if the smoke is not inhaled, may be worthwhile if they prove to be a comfort to the patient, and they may aid digestion.

THE COLON. For the first few days it is best to leave the bowels alone. An enema can then be given. Thereafter a muscle stimulant such as cascara may be given if it is needed. Saline purgatives should be avoided since they are apt to form gas

VITAMINS. Acute deficiency of vitamin B in beri-beri leads to a condition indistinguishable from heart failure (see p. 109). But it is rare, and in the treatment of heart failure proper this vitamin has no place. Ascorbic acid is a mild diuretic. Minor deficiencies are common and may lead to some anæmia. Orange juice should be included in the diet; if the plasma ascorbate is low, ascorbic acid should be given.

aimed merely at reducing the load of the heart muscle and improving its nutrition, so that it can again meet the needs of the body. Life must therefore be lived at a lower level, well within the compass of the heart.

Graduated exercises will now serve a double purpose. They will enable the patient to discover the distance he can walk without shortness of breath; and he can be instructed not to exceed it. They will also train the heart. The heart, like any other muscle, is capable of better performance if it is being used than if it is never required to do more than a bare minimum. The distance that the patient is able to walk without discomfort, when he starts his walking exercises, is no criterion of what he will be able to manage later. A system of graduated exercises gives him confidence in himself, and enables him to take an intelligent interest in his own welfare. It prevents him falling into the two dangerous extremes, either of taking no precautions at all, and so killing himself rapidly, or of becoming a chronic cardiac cripple, unable to move unassisted, a misery to himself and to his associates.

The patient can go for walks in selected areas, such as public parks, where there are usually suitable slopes and seats. He then learns how much he can do, and slowly regains his greatest capacity for exertion.

Patients who have recovered from heart failure should have their weight taken regularly. A sudden increase of a few pounds suggests a search for pulmonary congestion, hydrothorax, or peripheral œdema. A few days *should* then be spent in bed with neptal either orally or by injection. Many patients benefit from spending one day each week in bed during which mental relaxation as well as physical rest should be encouraged. In co-operative patients the return of œdema to any extent should be prevented, and the patient should never become water-logged

CARDIAC CACHEXIA. Patients whose life has been prolonged through careful treatment often *enter* a terminal phase of cardiac cachexia. All desire for food is lost and the weight steadily falls. No treatment avails, but death is usually sudden, presumably from ventricular fibrillation.

Prognosis. When *the heart* has failed the ultimate prognosis is bad But in many cases there is scope for limited optimism, and the attitude should always be hopeful. Social and economic

29 Brown, Friedfeld, Kissin, Modell, Sussman (1942) *J Amer med Assn*, 119, 1004
30 Wexler, Ellis (1944) *Amer Heart J*, 27, 86
[illegible]
42 Lewis (1928) *Brit med J*, 2, 977
43 Daley (1945) *Brit Heart J*, 7, 101
44 Howarth, McMichael, Sharpey-Schafer (1947). *Clin Sci*, 6, 187.
45 Sharpey-Schafer (1946) *Brit med J*, 2, 888.

Classification. In considering the classification and diagnosis of arterial diseases it is convenient to select certain points, much on the lines of the "four point" diagnosis of heart disease (1). This will bring the important features under review.

1. Etiological. Unfortunately, in a number of instances this will remain blank.
2. Anatomical. Here should be included the type of vessel and the part of the body or tissue in which it is found, and the pathological changes in it.
3. Physiological Impairment. Under this heading is included the liability to claudication, spasm, and the amount of vascular reserve for dilatation.
4. Functional Capacity. The degree of clinical derangement or disability.

Clinical Examination. The arteries should be carefully palpated, where they are accessible. Their thickness, tortuosity, and pulsation are noted The examination is best done when the limbs are reasonably warm The pulsation in one dorsalis pedis artery may be absent in about 12 per cent of healthy young men, and in one posterior tibial in about 2 per cent. It may be absent in the dorsal artery in about 7 per cent on both sides. This variation in normal persons must be remembered in examining those who are abnormal (2).

The skin is examined for trophic changes, elasticity, thinness, scaling, colour, the state of the nails, the return of blood when driven away by pressure If these points are studied in normal persons, abnormalities will be *more* readily appreciated.

Estimation of Arterial Function Much attention has been given to methods for assessing the degree of impairment in the arterial supply and to the estimation of the relative importance of the parts played by organic obstruction and vasomotor tone. The ability of the vessels to dilate needs careful study. Simple clinical means when aided by some experience in their use, will provide most of the information wanted Vasodilatation may be effected by the following methods —

1 Changes in Posture. The patient should be on a bed in a warm room. The *leg is then* elevated to 45°, and the rate of blanching is noted. In pathological states this is complete in a few seconds.

b. Hot Reaction Test. The subject sits in a room at a constant temperature of about 65°F. The temperature of the digits is read several times until it is constant, over about twenty minutes. One arm is immersed in a bowl of hot water, at 45°C., from the middle of the biceps to the middle of the hand. The temperature of the ends of the fingers is read on both sides After a short latent period there should be a rise of three or four degrees centigrade (6).

c Cutaneous Histamine Test. The skin is needled through a drop of 1/1000 histamine and a wheal is awaited. This should appear in five minutes in a normal limb. A delayed or negative result may indicate poor prospects of healing if amputation is contemplated.

4. SPINAL ANÆSTHETIC. The administration of a spinal anæsthetic will allow maximum vasodilatation by eliminating vasomotor tone; it reproduces temporarily the effect which should result from successful sympathectomy (7). There should be a rise in the cutaneous temperature of the toes of at least four degrees centigrade.

It is not uncommon to find the responses different in the two legs, although they may appear to be in the same condition.

5 PERIPHERAL NERVE BLOCK. The ulnar, or the peroneal or posterior tibial nerves can be blocked with procaine (3). It is necessary to block both the common peroneal and posterior tibial nerves in order to get a reliable result for the legs (8).

The elimination of spasm is important, for ischæmic pain on walking may be due to this alone (9). Gangrene is not likely, but the disability may be severe enough to warrant lumbar sympathectomy (10).

6. INTRAVENOUS INJECTION OF SODIUM NITRITE. After an injection of 1 c.c. of a 4 per cent solution the arterial pulsation in the limb is measured by means of the oscillometer (11). This test is said to be better than the test with heat for eliminating spasm in functional ischæmia.

7. OSCILLOMETRY. By this means it is possible to ascertain approximately the level of the arterial occlusion, and investigate pulses that cannot be palpated. The degree of pulsation . . . measured . . .

The patient should then stand. Normally the veins will fill in ten seconds. In pathological states there is delay in filling and flushing. The foot may become red in thirty seconds (3).

2. Reactive Hyperæmia. This is a modification of a test originally described by Moschcowicz. When the limb is warm, it is raised for thirty seconds to drain out the blood. A tourniquet is then applied to the thigh and the femoral artery occluded by inflating the cuff for four minutes, during which time the limb is kept warm. On sudden release of the tourniquet a flush should spread down to the toes in about fifteen seconds. The delay of the flush may be as much as three minutes when the arteries are occluded (4).

3. Tests of Skin Temperature. It is important to find out how far the vessels can dilate when the vasoconstrictor tone is eliminated, for this gives an opportunity of assessing the relative degrees of spasm and organic obstruction. This procedure is necessary before deciding on the value of operative interference.

The temperature of the skin of a limb is a good index of the amount of blood flowing through it, and the rise of temperature is an index of the capacity of the vessels to dilate. The temperature of the skin is recorded before and after induced vasodilatation. A skin thermometer is necessary, and for accurate work a thermocouple should be applied. By this means the temperature of any digit can be read accurately on a calibrated scale by the movement of a beam of light actuated by the deflection in a galvanometer.

a. Cold Reaction Test. The subject sits quietly, for not less than twenty minutes, in a room thermostatically controlled at 65° F. The temperature of each hand is then taken by holding the wire junction of the thermo-electric skin thermometer between the terminal pads of thumb and middle finger. This particular site is chosen because of the dense anastomotic bed in the finger tips, where any circulatory change is rapidly reflected in the temperature. Several preliminary readings are taken at intervals to ascertain the temperature level at rest. Then one hand is immersed covering the underside of the forearm to the elbow for one minute in water at 15° C. It is then removed and dried by dabbing with a towel to avoid friction. Temperature readings are resumed on both hands and recovery curves plotted. There is usually a fall of eight degrees centigrade in the immersed hand (5).

excruciating severity. It is out of proportion to the degree of ischæmia (1). Then small superficial blebs may be seen, often near the toe nails, or dry dull patches of skin, or some tiny abrasion fails to heal. Later arterial pulsation disappears, and the tests of arterial function show grave deficiences The infective process may lead to local gangrene and sloughing.

The course of the disease is very slow and marked by considerable remissions of long duration.

Pathology. The lesion consists of an inflammatory process involving all three coats of the artery. All three coats are infiltrated with polymorphs; the normal structure is lost, and clot fills the lumen. Recanalisation may be seen after an interval. The adjacent vein undergoes phlebitis and the nerve nearby may be involved Finally all three become matted together by fibrous tissue. The artery may be completely obliterated. The fibrosis, infiltration, and Wallerian degeneration of the nerves, with thrombosis of their vasa nervorum, introduces an important neuritic factor (2).

The valves of the veins become disorganised, and inflammation and thrombosis may cause obstruction with dilatation distally (3). The skin becomes thin, shiny, dry and scaly. There is discolouration, blebs form and become infected. The nails are brittle and do not grow. Any lesion fails to heal.

The deprivation of blood leads to trophic changes. These probably come fairly late, when the flow has been reduced to one third of the normal (4). The chief trouble is the *progressive* arterial obliteration. The earlier vasomotor changes are not so important (5).

No significant changes in the blood chemistry have been noted (6). Although the conspicuous lesions are found in the arteries of the legs, and to a lesser degree of the arms, other arteries may be affected too. Coronary thrombosis is common, and may cause death (7). But the lesions are not necessarily those of thrombo-angeitis. Cerebral lesions have been recorded, transient at first, leading finally to permanent hemiplegia (8). Occasionally thromboses have been found in the mesenteric arteries, causing acute abdominal pain

Prognosis. The outlook is bad, although the course may be long. In one series the average length of life was twelve years. Vascular accidents ...

EXAMINATION WITH X-RAYS. An ordinary skiagram will sho medial calcification.

INJECTION OF RADIO-OPAQUE SUBSTANCES. (18 cc of 25 p cent diodrast solution)

Thorotrast or diodrast can be used by intra-arterial injecti (13) There are dangers connected with thorotrast which mak it undesirable This method has been used for study of the arteri other than those in the limbs A 50 per cent solution of *diodra* (10-12 cc) has been injected into the common carotid artery t show the cerebral arteries (14). Perabrodil (6-10 cc of 35 per cen solution for *intravenous injection) has been used also, and show* aneurysms well (15)

REFERENCES

1 SALAND *et al* (1940) *Arch intern Med* **65** 1035
2 SILVERMAN (1946) *Amer Heart J* **32** 82
3 MONTGOMERY *et al* (1941) *Amer Heart J* **21** 780
4 PICKERING (1933) *Brit med J* **2** 1106
5 WOODMANSEY (1940) *Annals of Rheumatic Dis* **5** 99
6 BENATT TAYLOR (1940) *Brit Heart J* **2** 281
7 TELFORD STOPFORD (1932) *Brit med J* **1** 1116
8 SALAND *et al* (1945) *Amer Heart J* **30** 398
9 LEARY ALLEN (1941) *Amer Heart J* **22** 719
10 PEARL (1937) *Amer J med Sci* **194** 505
11 GROOTNIK *et al* (1942) *J Lab clin Med* **27** 878
12 ATLAS (1939) *Arch intern Med* **63** 1158
13 SANCHEZ PEREZ (1941) *Surgery* **10** 535
14 GROSS (1941) *Radiology* **37** 487
15 ENGERSET (1944) *Acta radiologica Supp* **66** 166

Thrombo-Angeitis Obliterans (Buerger's Disease)

This disease is almost exclusively confined to males Cigarette smoking appears to favour its development and there is a tendency to a higher incidence among Jews The true cause is unknown The arteries of the legs are affected more than those of the arms and the veins and nerves are involved as well The onset is usually early in adult life between the ages of fifteen and forty Early in the illness there are fleeting phases of the Raynaud phenomenon Pains are felt in the soles toes and ankles, these come on during walking. Cramps occur in the muscles of the feet and calves One leg is usually affected before the other At this stage pulsation is still felt in the main arteries The colour changes on alterations in posture may be abnormal The feet tend to feel cold. Pain at rest tends to become persistent and severe and may be of

These were only immediate results of one test, and it is pointed out that they do not exclude some ultimate effect after repeated use

DRUGS Vasodilators have little value. Nicotinamide does not seem to be really effective (14, 15). Papaverine two to four grams by mouth, is probably as useful as anything else for alleviating the pain of intermittent claudication and affording some improvement in walking.

Abstention from tobacco is certainly important. Nicotine causes some degree of vasoconstriction in most people.

SYMPATHECTOMY. If, in spite of treatment, the disease progresses relentlessly, as it so often does, sympathectomy must be considered. The value of this depends entirely on the possibility of increasing blood flow by eliminating vasomotor tone; so that in a disease where an obliterative process is at work the effect may not be great. For the legs lumbar ganglionectomy, including L_2, is the rule. It is important to gauge the possibilities of vasodilatation, and to what extent collateral circulation is present. This can be done by observing the results of a spinal anaesthetic on the skin and temperature.

The cases with advanced trophic changes, severe pain, pronounced blanching on exertion and blueness on lowering the limb, particularly after a recent exacerbation, are likely to afford unsatisfactory results. The collateral circulation may be bad, and as a result of the sympathectomy blood may be shunted elsewhere (16). By this method temporary relief may undoubtedly be obtained, even if the course of the disease is not materially changed. Many can for a time return to work, and they are usually young The nature of the occupation needs consideration and other measures will help (17).

Gangrene should be treated as conservatively as possible. Hypertonic saline is useful. Relatively good recovery is often achieved by this means with less loss of tissue than at first seemed likely.

REFERENCES

1 HINES (1938) *Proc Staff Meet Mayo Clin*, 13, 694
2 BARKER (1938) *Arch intern Med*, 62, 271
3 EDWARDS, E, EDWARDS, J (1943) *Arch Path*, 35 242
4 STEAD, KUNKEL (1938) *J clin Invest*, 17, 715.
5 LANSDOWNE (1942) *Amer. Heart J.* 24 50
6 ROTH, *et al* (1938) *Arch intern Med*, 62, 413
7 FATHEREE, HINES (1938) *Proc Staff Meet Mayo Clin* 13, 249

series of nearly a thousand patients (of whom 95 per cent were smokers) amputation was needed in 30 per cent in three years, 40 per cent in five years, and 60 per cent within ten years (10).

Treatment. This must aim at keeping the skin healthy and protecting from trauma, and improving the circulation. When the skin is dry, the use of oil at night and dusting powder in the day, is advisable. Socks and shoes must fit well. Great care is needed with the nails, and any corns or bunions. In the acute phase rest will be essential. Exposure to cold must be avoided. Septic foci should be cleared up.

Exercises. The circulation can be improved by raising and lowering the limb. The patient is recumbent. The leg is raised to about 70° and supported there until it blanches. It is then lowered over the edge of the bed until it is thoroughly flushed. Lastly, it is brought back to the horizontal. The cycle may be repeated for an hour. Two or three such courses of treatment may be given every day.

Passive Congestion (venous occlusion) Intermittent occlusion of the veins for a few seconds at a time helps to produce engorgement and increase collateral circulation (11). The patient can do this for himself with a sphygmomanometer bag. The pressure should be raised to 60 mm. Hg. for two minutes and released for four minutes. The cycle can be repeated during half an hour. Experimental evidence shows that the increase in flow is related to the height of the pressure in the veins up to a point. Then it decreases (12)

Intermittent Suction and Compression. By means of suitable apparatus (Pavaex Unit) a positive, alternating with a negative, pressure can be exerted on the limb, with the aim of increasing the vascular bed

Intravenous Injections. Large doses (250 cc.) of normal saline, or sometimes slightly hypertonic saline (2 to 5 per cent) have been given intravenously They may be given every two or three days. Magnesium sulphate (10 per cent) has also been used, and sodium citrate 2 per cent, or sodium iodide 2 per cent.

Investigation with the plethysmograph showed that intravenous hypertonic saline produced some increase in flow in one-third of the cases. Padutin had very little effect. Intermittent venous occlusion was likewise ineffective (13).

These were only immediate results of one test, and it is pointed out that they do not exclude some ultimate effect after repeated use.

DRUGS. Vasodilators have little value. Nicotinamide does not seem to be really effective (14, 15). Papaverine two to four grains by mouth, is probably as useful as anything else for alleviating the pain of intermittent claudication and affording some improvement in walking

Abstention from tobacco is certainly important. Nicotine causes some degree of vasoconstriction in most people.

SYMPATHECTOMY. If, in spite of treatment, the disease progresses relentlessly, as it so often does, sympathectomy must be considered. The value of this depends entirely on the possibility of increasing blood flow by eliminating vasomotor tone; so that in a disease where an obliterative process is at work the effect may not be great. For the legs lumbar ganglionectomy, including L_2, is the rule. It is important to gauge the possibilities of vasodilatation, and to what extent collateral circulation is present. This can be done by observing the results of a spinal anæsthetic on the skin and temperature.

The cases with advanced trophic changes, severe pain, pronounced blanching on exertion and blueness on lowering the limb, particularly after a recent exacerbation, are likely to afford unsatisfactory results. The collateral circulation may be bad, and as a result of the sympathectomy blood may be shunted elsewhere (16) By this method temporary relief may undoubtedly be obtained, even if the course of the disease is not materially changed Many can for a time return to work, and they are usually young The nature of the occupation needs consideration and other measures will help (17).

Gangrene should be treated as conservatively as possible, Hypertonic saline is useful. Relatively good recovery is often achieved by this means with less loss of tissue than at first seemed likely.

REFERENCES

1 HINES (1938) *Proc Staff Meet. Mayo Clin*, 13 694.
2 BARKER (1938) *Arch intern Med*, 62, 271
3 EDWARDS, E., EDWARDS, J (1943) *Arch Path*, 35, 242
4 STEAD, KUNKEL (1938) *J. clin Invest*, 17 715
5 LANSDOWNE (1942) *Amer. Heart J.* 24, 50
6 ROTH, *et al* (1938) *Arch intern Med*, 62, 413.
7 FATHEREE, HINES (1938) *Proc. Staff Meet. Mayo Clin*, 13, 240

8. ANTONI (1941). Acta Med Scand., 108, 502
9 AVERBUCK, SILBERT (1934) Arch intern. Med, 54, 436.
10 HORTON (1938). J. Amer med Ass, 3, 2184
11. KRAMER (1939) Amer J med Sci, 197, 808.
12. LINTON (1941) Amer Heart J, 21, 721
13 ABRAMSON (1941) Amer Heart J, 21, 756
14. BEAN, SPIER (1940) Amer Heart J, 20, 62
15 ABRAMSON, et al (1940) Amer J med Sci, 200, 96
16. ATLAS (1942) Amer Heart J, 23, 492
17. DE TAKATS (1944). Surg Gyn Obst, 79, 359

Polyarteritis (Periarteritis) Nodosa

(Kussmaul's Disease)

This disease, characterised by widespread nodules on the arteries throughout the body, presents a protean clinical picture. There are, on the one hand, the general symptoms, and on the other, special local indications of arterial inflammation, leading to ischæmic changes in the areas they supply.

General Symptoms. Men are affected considerably more frequently than women, perhaps ten times as often. The disease tends to appear in the early years of adult life, but may be met with in old people as well. The onset is insidious as a rule. Occasionally it is sudden, particularly if some unexpected arterial catastrophe, often intra-abdominal, reveals what is probably a latent process. There is fever, varying in height and running a persistent course; with this there is usually severe constitutional disturbance, marked by tachycardia, sweating, great lassitude, and pains about the body, particularly in the muscles and the joints. The patient becomes obviously seriously ill, tends rapidly to lose weight, and exhibits profound debility (1). Anæmia becomes obvious but is not severe. There may be some enlargement of the spleen and liver: occasionally there is troublesome bronchitis and bronchiolitis (2). These general symptoms are not likely to provide a diagnosis. At a varying interval after the onset the different manifestations of local disturbance appear. Singly they may lay a false scent, but when enough are present together the picture becomes more clear.

Local Arteritis. In this disease the grosser lesions affect the internal arteries as a rule, and so they cannot be palpated. But sometimes nodules can be felt on palpable arteries, such as the brachial, about half a centimetre across, and rather tender. This arteritis does not attack the temporal arteries particularly. The

arteries may thrombose or develop aneurysms. The lesions of the internal arteries can only be inferred from their secondary effects. There may be intermittent claudication.

MUSCLES. They are painful, with what seem to be rheumatic pains from the onset. They may be acutely tender. Wasting may set in, and there may be loss of faradic reaction. Weakness may become conspicuous in various muscle groups, causing *foot or* wrist drop.

NERVES The symptoms are those of a peripheral *polyneuritis*. There may be paræsthesia and anæsthesia; this peripheral neuritis is no doubt linked up with the motor weakness, although there are lesions in arterioles of the muscles too. Reflexes are lost erratically about the body. The vasa nervorum show lesions which cause this peripheral neuritis.

SKIN AND SUBCUTANEOUS TISSUES. Occasionally small split-pea nodules can be felt in the skin, but these are rare. Sometimes they are very profuse and remarkably evanescent (2). More conspicuous are areas of subcutaneous pitting œdema, often quite extensive on the limbs and about the body. These may be associated with the muscular weakness (3). Purpura may be noted, sometimes extensive; and symmetrical in distribution. The smaller *joints* may be swollen and painful.

VISCERAL SYMPTOMS. Acute abdominal pain may lead to laparotomy (4) The gall bladder has been found to be the site of acute disease (5) Ulcers have been *found in the alimentary* tract. Hæmorrhages may occur from ruptured vessels, such as the splenic or renal arteries (6).

Thrombosis of mesenteric vessels may cause severe pain and distension, simulating intestinal obstruction. Melæna may be severe, or there may be frank blood. As mentioned, the liver and spleen may become enlarged

RENAL LESIONS. These are very important They may affect the main renal artery and cause obstruction or aneurysm, which may rupture; or thrombosis may lead to ischæmia and the Goldblatt type of ischæmic hypertension; or they may affect the smaller branches or even the intrarenal arterioles.

Hæmaturia and albuminuria are very common, *in fact the* appearance of nephritis may predominate, even to uræmia (7). A peculiar sediment has been described in the urine, consisting of

red cells, granular and fatty casts, fatty bodies, blood casts, associated with much protein (8).

CARDIAC LESIONS. The coronary arteries may be attacked, and myocardial infarction result (7). This is not infrequent. Hypertension is common; some say almost invariable at one time or another (9). No doubt it is connected with the renal lesion. Retinal lesions are rare, but conjunctivitis is not uncommon: the arteries in the lungs usually tend to escape, but transient areas of consolidation like pneumonia may be found in the lungs, and there may be hæmoptysis (16).

Course and Prognosis. The course is usually long, anything from six months to two years, or even more, and the prognosis is very grave. Heart failure and renal failure may come on; there is often cerebral hæmorrhage. Contractures may cripple the muscles.

Laboratory Investigations. All cases show a certain degree of leucocytosis. Eosinophilia is not so common as once supposed, but may be high. It may be due to causes other than the disease, particularly asthma (10). There is usually moderate anæmia. The blood sedimentation rate may be a great deal raised. The blood urea may rise. The Wassermann is negative. The serum albumen may be raised (3). Biopsy is always worth while. A piece of muscle near an œdematous area, or one which is tender and painful, or a nodule if available, should be taken. Blood culture is consistently negative.

Ætiology. Nothing is definitely known. There is possibly an association with asthma to suggest further an allergic basis. The acute necrotic lesions in the arterioles and arteries are unlike other disturbances due to allergy (10). It has been claimed that anaphylactic reactions to foreign serum, and sulphonamides (11), and also iodine (12) have provoked the disease. Sensitivity to arsenic has been blamed, for cases have been reported which have arisen during treatment for syphilis with organic arsenical preparations (15). One is struck by the very different nature of these various antigens; where so much variety exists there must be other causes in the patients, which have more in common.

Pathology. The initial lesion is an acute medial necrosis, marked by hyaline changes. Possibly in larger arteries this comes about from lesions obliterating the vasa vasorum. There is

cellular infiltration in those areas, polymorphs being numerous. There is intimal proliferation, leading often to thrombosis. The adventitia is infiltrated too. The arterial coats may be so damaged that an aneurysm forms, which may rupture. Macroscopically small whitish nodules on any of the internal arteries may be seen. Microscopical lesions are often present when nothing is visible to the naked eye. Infarcts may be seen almost anywhere, as a result of the obstructions in the arteries. Gangrene may result.

Differential Diagnosis. It will be seen that a disease with such a multitude of clinical variations must be hard to diagnose, until some definite local lesion develops. Nephritis, peripheral neuritis, myositis, some acute abdominal lesion, coronary thrombosis, may all have to be considered. As is usual with widespread lesions, the association of several incongruous, unusual and apparently unrelated features may bring the possibility to mind, in a patient who is obviously very ill, with an infective type of disease.

There is no effective line of treatment at present. Sulphonamides would seem to be contra-indicated. The possibility of some association with temporal arteritis, and disseminated lupus erythematosus, scleroderma, dermatomyositis and the Libman-Sacks disease may be shown by future studies of this group of rare diseases.

REFERENCES

1 LICHTMAN, STOCKMAN (1943) *Proc Staff Meet Mayo Clin*, **18**, 500

Temporal Arteritis

This uncommon disease was described first by Horton, Magath and Brown in 1932 (1). The affection appears to be more likely to affect women than men. The patients are elderly or old. The symptoms may be classified as general and local. The insidious onset is usually marked by the general disturbances which may precede by months the development of the local lesion which has given its name to what is certainly a widespread disease affecting the whole arterial system. The patient falls ill, with fever, sweating, and indefinite pains in muscles and joints. There is progressive loss of weight, which may reach a severe degree, so that when the disease is well established the patient may really be very ill indeed. Headache may be intense and prolonged, and present an early obscure symptom. It may be due either to intracranial lesions, or directly to the inflamed superficial arteries. The conspicuous lesion is a swollen thickened nodular temporal artery, intensely tender, which is the source of severe pain. Its pulsation is diminished. The skin over it becomes red and there may be local œdema. One to three inches of its course may be affected. Similar affection may be found in the occipital or posterior auricular arteries. Difficulty in opening the jaw is common and may seriously interfere with eating. (2, 3). The cervical glands may be enlarged and tender. In some cases the disturbance is slight as regards general health, and the local lesion mild.

Cerebral Symptoms. *Headache, vertigo, nausea and vomiting* may almost simulate cerebral tumour. Mental sluggishness and confusion (4), delirium (5), and coma may supervene (6)

Eye Symptoms. Photophobia (7) and varying degrees of loss of vision amounting sometimes to blindness may develop. The ophthalmoscope shows swelling of the disc, obliteration or ischæmia of the arterioles, and the areas they supply, hæmorrhages, or atrophy of the disc (8). Both eyes may be affected. Ptosis has been noted.

Arterial Lesions. Apart from those in the scalp and retina, and, presumably, brain, arteritis has been noted in the arms and the legs. The associated veins have also been involved (9).

There does not appear to be any constant elevation of the blood pressure. There is usually moderate anæmia and leucocytosis. The sedimentation rate is raised, sometimes to a high degree. A

rise in the protein content of the cerebrospinal fluid has been noted. The urine usually seems to be normal. The Wassermann reaction is negative.

Pathology. The lesions are characteristic and can easily be studied by biopsy of the temporal artery. An inflammatory process spreads in from the adventitia and develops in the middle coat. Focal necrosis appears first, and is followed by the growth of granulation tissue, in which giant cells are conspicuous (11) The inflammation appears to spread along the vessel. The elastic coat may disappear, or new layers may be laid down. The intima shows proliferation and the lumen thrombosis.

There is distribution of these lesions throughout the arterial system. Most of the large arteries were affected in some autopsies including the aorta (11, 12) The kidneys may be affected too, and also the coronary arteries (9).

The cause is unknown. Focal sepsis in teeth and sinuses has been suggested, and there may possibly be some link with the former, for extraction of teeth has apparently relieved some patients and caused exacerbation in others (14).

Prognosis. The disease may run a course lasting many months, but most cases appear to recover in the end, even though the patient has appeared very ill at its height.

TREATMENT. Some relief of pain is afforded by excising the inflamed temporal artery (10)

It is evident that this is a generalised disease affecting all the arterial system. In some respects it may resemble polyarteritis nodosa. They have in common myalgic pains, arthralgia, and arterial lesions The distribution of these is different, being more visceral in polyarteritis. Here there is polyneuritis, more severe renal involvement, and a bad prognosis. Headache and ocular symptoms are not conspicuous. Thrombo-angeitis obliterans affects more the peripheral arteries of the limbs, in particular of the legs, and involves the veins and nerves; there is more widespread inflammation through all three arterial coats. The disease is almost exclusively confined to men.

The histological changes of periarteritis may be difficult to distinguish from those of temporal arteritis. On the whole, they are more suppurative and destructive, and the giant cells are less conspicuous (9, 14).

Temporal Arteritis

This uncommon disease was described first by Horton, Magath and Brown in 1932 (1). The affection appears to be more likely to affect women than men. The patients are elderly or old. The symptoms may be classified as general and local. The insidious onset is usually marked by the general disturbances which may precede by months the development of the local lesion which has given its name to what is certainly a widespread disease affecting the whole arterial system. The patient falls ill, with fever, sweating, and indefinite pains in muscles and joints. There is progressive loss of weight, which may reach a severe degree, so that when the disease is well established the patient may really be very ill indeed. Headache may be intense and prolonged, and present an early obscure symptom. It may be due either to intracranial lesions, or directly to the inflamed superficial arteries. The conspicuous lesion is a swollen thickened nodular temporal artery, intensely tender, which is the source of severe pain. Its pulsation is diminished. The skin over it becomes red and there may be local œdema. One to three inches of its course may be affected. Similar affection may be found in the occipital or posterior auricular arteries. Difficulty in opening the jaw is common and may seriously interfere with eating. (2, 3). The cervical glands may be enlarged and tender. In some cases the disturbance is slight as regards general health, and the local lesion mild.

Cerebral Symptoms. Headache, vertigo, nausea and vomiting may almost simulate cerebral tumour. Mental sluggishness and confusion (4), delirium (5), and coma may supervene (6).

Eye Symptoms. Photophobia (7) and varying degrees of loss of vision amounting sometimes to blindness may develop. The ophthalmoscope shows swelling of the disc, obliteration or ischæmia of the arterioles, and the areas they supply, hæmorrhages, or atrophy of the disc (8). Both eyes may be affected. Ptosis has been noted.

Arterial Lesions. Apart from those in the scalp and retina, and, presumably, brain, arteritis has been noted in the arms and the legs. The associated veins have also been involved (9).

There does not appear to be any constant elevation of the blood pressure. There is usually moderate anæmia and leucocytosis. The sedimentation rate is raised, sometimes to a high degree. A

Distribution. There is a tendency for the most severe lesions to be found in the abdominal aorta. The scar of the ductus Botalli, and the spot where the intercostals leave, are favourite sites. Whether this is due to local currents, or mechanical stresses from the pulse wave is not known. The coronary arteries are, of course, notoriously prone, and so are the cerebral. Whatever causes operate, singly or in combination, the following process is established. The cholesterol esters are engulfed by phagocytic cells in the subintimal tissues. Small raised yellow streaks can be seen macroscopicaly. Possibly there is a positive chemotaxis favouring the deposit of these substances. There then follows a local reaction of overgrowth due to irritation (1). The intima becomes thickened over the deposits. Later these calcify, or soften and break down.

Results. Two important results finally develop. If the artery is small, obstruction of its lumen may impair the function of the tissues it should supply, as in the myocardium, the brain, or the kidneys. The presence of the lesions favours thrombosis, as in the coronary or cerebral arteries.

In addition, atheroma may affect the heart valves. It is quite common in the anterior cusp of the mitral (2). But there is little *thickening* Similarly, the aortic cusps are sometimes affected at their bases. Both *may calcify*, but the function of the valves is not as a rule much affected. The fibrocalcareous stenosis of the aortic valves is probably another sort of lesion altogether (*p. 61*).

Diagnosis. In most cases the *presence of* the lesions can only be inferred by their effects, as in the coronary arteries. The presence of atheroma in one place is no indication of its presence in another Radiology *may help* [illegible]
is often seen at the back of [illegible]
joined it. Calcification may [illegible]
of the shadow elsewhere. Apart from calcification, possibly some increase in the density of the shadow may be detectable. Examination of the palpable arteries gives no clue to the presence of atheroma. Except for its tendency to provoke local ischæmia, this pathological process is not in itself the cause of serious consequences.

Mönckeberg's Degeneration. The characteristic lesion is a calcification of the middle coat. This is found in the medium-sized

REFERENCES

1. Horton, B T, Magath, T. B, Brown, G. E (1932). *Proc. Staff Meet Mayo Clin*, 7, 700
2. Brown, J W, Hampson, F (1944) *Brit Heart J*, 6, 154.
3. Dick, G F, Freeman, G (1940) *J Amer med Ass*, 114, 645
4. Sprague, P G, MacKenzie, W C (1940) *Can Med, Ass J*, 43, 526
5. Schaefer, C L, Sanders, C E (1942) *Amer Heart J*, 24, 410.
6. Chasnoff, J, Vorzimmer, J J (1944) *Ann intern Med*, 20, 327
7. Bain, C W C (1938) *Lancet*, 1, 517
8. Johnson, R H Harley, R D, Horton, B T (1943) *Amer J Opth*, 26, 147
9. Jennings (1938) *Lancet*, 1, 424
10. Cooke, W T, *et al* (1946) *Quart J Med* 15, 47
11. Bowers (1940) *Arch intern Med*, 66 384
12. Gilmour J R (1941) *J Path Bact* 53 263
13. Sproul E E (1942) *New York State J Med* 42, 345
14. Kilbourne, Wolff (1946) *Ann intern Med*, 24, 1

Degenerative Arterial Disease

Atheroma (Atherosclerosis). Atheroma is a local degenerative process. Deposits of cholesterol esters collect in the subintimal tissues of the larger internal arteries There are several causes which may lead to its deposit. The first is time. Atheromatous deposits are first detected quite early in life, and as age advances they become more extensive The second is pressure. The wear and tear of a raised pressure seems to favour it. This is notably so in the pulmonary arteries, where atheroma is rare unless the pressure is raised, as in mitral stenosis and some forms of pulmonary disease. Systemic hypertension favours the development of atheroma, but the relationship is not constant; it may be extensive although the blood pressure is low. Cholesterol circulates in the blood stream and is the source of the deposits. Hypercholesterolæmia would theoretically tend to cause them, but here again the relationship is vague. The disease is not more conspicuous in some conditions, such as chronic glomerulo-tubular nephritis, where there is a high cholesterol level But perhaps the time factor is inadequate. The artificial production of atheroma in rabbits has been achieved by feeding with cholesterol, but the parallel is not very close in man. The predisposition may be in the subintimal tissues: there seems to be an inherited liability to the disease, "the inherited bad tubing" of Osler. The distribution of the lesions seems to depend on local mechanical factors, but it is not clear what they are. Diabetes appears to predispose to the development of atheroma. The arterioles are immune, and the arteries of the limbs tend to escape, except proximally.

Distribution. There is a tendency for the most severe lesions to be found in the abdominal aorta. The scar of the ductus Botalli, and the spot where the intercostals leave, are favourite sites. Whether this is due to local currents, or mechanical stresses from the pulse wave is not known. The coronary arteries are, of course, notoriously prone, and so are the cerebral. Whatever causes operate, singly or in combination, the following process is established. The cholesterol esters are engulfed by phagocytic cells in the subintimal tissues. Small raised yellow streaks can be seen macroscopicaly. Possibly there is a positive chemotaxis favouring the deposit of these substances. There then follows a local reaction of overgrowth due to irritation (1). The intima becomes thickened over the deposits. Later these calcify, or soften and break down.

Results. Two important results finally develop. If the artery is small, obstruction of its lumen may impair the function of the tissues it should supply, as in the myocardium, the brain, or the kidneys. The presence of the lesions favours thrombosis, as in the coronary or cerebral arteries.

In addition, atheroma may affect the heart valves. It is quite common in the anterior cusp of the mitral (2). But there is little thickening. Similarly, the aortic cusps are sometimes affected at their bases. Both may calcify, but the function of the valves is not as a rule much affected. The fibrocalcareous stenosis of the aortic valves is probably another sort of lesion altogether (p. 61).

Diagnosis. In most cases the presence of the lesions can *only* be inferred by their effects, as in the coronary arteries. The presence of atheroma in one place is no indication of its presence in another. Radiology may help. A crescent of calcified atheroma is often seen at the back of the arch where the ductus *arteriosus* joined it. Calcification may be seen as lines just within the border of the shadow elsewhere. Apart from calcification, possibly some increase in the *density* of the shadow may be detectable. Examination of the palpable arteries gives no clue to the presence of atheroma. Except for its tendency to provoke local ischæmia, this pathological process is *not in* itself the cause of serious consequences.

Mönckeberg's D[illegible]
calcif

arteries of the limbs, especially the legs, the posterior tibials in particular. Ossification may be found. With this is an associated proliferation of the intima, which favours the possibility of thrombosis. Study of the arteries in amputated limbs shows the remarkable extent to which these processes may develop. The formation of clot appears to be the final event, deciding gangrene (3). The thickening of the walls of the main channel obstructs the mouths of the branches leaving it. This disease is most commonly seen in old men, and is the cause of the intermittent claudication of the elderly. Senile gangrene of the extremities of the limbs is the final complication.

ASSOCIATION WITH DIABETES. There is no question that an association exists, just as with atheroma (4). Conversely, patients whose diabetes is controlled appear to be less likely to develop arterial disease (5). When trophic changes set in, the presence of diabetes aggravates them, and favours sepsis and gangrene.

TREATMENT. The principles are those given under thrombo-angeitis. As these patients are old, sympathectomy is hardly ever justified. The chances of improving collateral circulation are not good. Contrast baths, in which the legs are immersed in hot water for about ten minutes, and then in cold for two, may be tried. Many cases run a very slow course, the diminished activites of old age are more tolerant of inferior blood supply.

Simple Arteriosclerosis. It is better to reserve this name for arterial thickening which is not the medial hypertrophy of hypertension, nor the medial degeneration of Monckeberg, nor the subintimal lipoidystrophy of atheroma. It is unfortunate that so often it is employed indiscriminately for one or all of these. The difficulty arises that these special types may be present as well. As age advances the arteries show wear and tear. They tend to lose elasticity and stretch, so that they become tortuous. A certain amount of thickening is palpable due to fibrosis of the middle coat and some proliferation of the intima and elastica. These changes are more apparent in men, particularly those who have been manual labourers. While age is the chief association, this is very variable; some very old men have the arteries normal for a man twenty years younger, and the converse is frequent enough (6).

Kinking of the Carotid Artery. The right carotid artery in women may become kinked and somewhat dilated. The appear-

ance simulates an aneurysm. Most of these patients have hypertension; occasionally there is coarctation. Others are often obese and somewhat kyphotic. Usually the aorta is elevated and elongated, and the bifurcation of the innominate may be high. There is usually some atheroma, but not syphilis. Skiagrams show the shadow of the artery at the apex of the right lung. Patients may be worried by the pulsation, or conscious of its throbbing. The cause is purely dynamic. The condition is best left alone (7).

REFERENCES

1. LEARY (1941) *Arch. Path.*, 32, 507.
2.
3.
4.
5.
6.
7. PARKINSON, BEDFORD ALMOND (1939) *Brit. Heart J.*, 1, 345

Dissecting Aneurysm of the Aorta. This lesion was fully reviewed in Shennan's monograph in 1934 (1); since then a good many cases have been recorded filling in the details of a complex, but well recognisable clinical picture.

PATHOLOGY. The constant finding is the cystic medial necrosis

... cyst may easily be seen by the naked eye. Small lymphocytic areas may be found, and some degree of proliferation of fibrous tissue. The cause of this mucoid degeneration is unknown, but it has been suggested that there may be an excess of a mucoid substance normally present in mesoblastic structures (3). The intima and adventitia are normal. *Neither* syphilis nor atheroma are causes. The rupture may *finally* be precipitated by bleeding from a small vas vasorum. A rent occurs in the intima, most commonly in the *ascending* portion, or at the junction of the ascending and transverse; or at the junction of the transverse and descending parts of the arch. The tear is usually longitudinal in the first part and transverse higher up. (4).

The bloc...

up c

thre ... the aneurysm may rupture into the pericardial sac and cause a rapidly fatal tamponade by a gross hæmopericardium. The aorta may become dilated and an

arteries of the limbs, especially the legs, the posterior tibials in particular. Ossification may be found. With this is an associated proliferation of the intima, which favours the possibility of thrombosis. Study of the arteries in amputated limbs shows the remarkable extent to which these processes may develop. The formation of clot appears to be the final event, deciding gangrene (3). The thickening of the walls of the main channel obstructs the mouths of the branches leaving it. This disease is most commonly seen in old men, and is the cause of the intermittent claudication of the elderly. Senile gangrene of the extremities of the limbs is the final complication.

ASSOCIATION WITH DIABETES. There is no question that an association exists, just as with atheroma (4). Conversely, patients whose diabetes is controlled appear to be less likely to develop arterial disease (5). When trophic changes set in, the presence of diabetes aggravates them, and favours sepsis and gangrene.

TREATMENT. The principles are those given under thrombo-angeitis. As these patients are old, sympathectomy is hardly ever justified. The chances of improving collateral circulation are not good. Contrast baths, in which the legs are immersed in hot water for about ten minutes, and then in cold for two, may be tried. Many cases run a very slow course; the diminished activites of old age are more tolerant of inferior blood supply

Simple Arteriosclerosis. It is better to reserve this name for arterial thickening which is not the medial hypertrophy of hypertension, nor the medial degeneration of Monckeberg, nor the subintimal lipoidystrophy of atheroma It is unfortunate that so often it is employed indiscriminately for one or all of these. The difficulty arises that these special types may be present as well. As age advances the arteries show wear and tear They tend to lose elasticity and stretch so that they become tortuous. A certain amount of thickening is palpable due to fibrosis of the middle coat and some proliferation of the intima and elastica These changes are more apparent in men, particularly those who have been manual labourers. While age is the chief associ[illegible] is very variable; some very old [illegible] a [illegible]

[illegible] right carotid artery in [illegible] kinked and somewhat dilated. The appear-

of the innominate and subclavian may alter the pulses in the radials; involvement of the carotid causes syncope and paralysis (11). If the renal arteries are affected there may be anuria or hæmaturia (12).

The loss of the pulses in the legs is very important, and may provide the diagnosis. The limbs become pale and cold and bluish, and numb. All power is lost and the tendon reflexes are abolished (13). A murmur and thrill have been described over the femoral artery (14).

If the dissection spreads into the pericardial sac death occurs at once. Some interesting cases have been recorded where the coronary arteries have been affected. In one the left was obstructed and an infarct formed (15). The right has been obstructed and the electrocardiogram showed the changes due to posterior infarction (16, 17, 18). When this happens the diagnosis may be confused with coronary thrombosis.

In the root of the aorta the valves may be rendered incompetent, and new murmurs, systolic and diastolic appear. The left ventricle rapidly dilates and intractable failure may come on (19). There is usually some degree of leucocytosis and occasionally slight jaundice.

Radiology. The shadow of the aneurysm is usually seen on the left side of the chest. The outline may be irregular, and the density variable. Pulsation may be changeable from time to time or relatively slight (20).

Course and Prognosis. Probably nine cases out of ten die very quickly, from rupture into the pericardial sac, or less often into the left pleural sac (21). But it is clear that quite a number survive, and some surprisingly *long*; recovery may be very complete and activity at a normal level for some years [illegible]

[illegible] channel (25).

Diagnosis. The intensely severe pain, with its peculiar spread, may be characteristic. The loss of power and circulation in the legs, or the appearance of aortic murmurs and evidence here and there of pressure effects are the *positive points*. The abdominal pain and vomiting may simulate a surgical emergency, but the rigidity is not notable. The site of the pain may suggest coronary occlusion, but the cardiogram does not as a rule support it.

aneurysm form, without actual rupture in the ascending portion (5). Sometimes in addition to the main rupture, small multiple aneurysms are formed (6).

Spreading in the other direction the dissection may even reach the popliteal arteries (7) Sometimes a double tube is formed, a false aorta, and the blood reaches the true aorta again in the abdominal region. Rupture may occur into the left pleural sac. This is usually rapidly fatal, but survival with a hæmothorax and death from a second rupture after some months has been recorded (26)

It will be seen that when a lesion such as this spreads so widely a great variety of effects may be produced. The aneurysm may exert pressure on adjacent structures, or the blood supply to organs may be interfered with.

CLINICAL FEATURES Men are affected twice or thrice as often as women The disease is very rare under the age of forty, but it has occurred at fifteen (7). Almost all patients have high blood pressure. The onset is sudden, and often associated with physical strain or emotional disturbance

Pain of excruciating intensity, of a rending, tearing character, comes on suddenly, usually in the precordial area, sometimes in the back, and occasionally in the abdomen, or lumbar region. It tends to spread from the front to the back, or vice versa, and down from the chest to the abdomen, and into the legs. There may be radiation to the neck, but not often to the arms. In spite of the pain, the abdominal muscles are not particularly rigid. The pain may persist for days. Occasionally there is no pain (23); the patient develops heart failure with a aortic reflux due to enlargement (8) There is commonly *shock and collapse*, so that the blood pressure falls, which may be misleading (9). Vomiting is usual and may be severe.

PRESSURE ON ADJACENT STRUCTURES. Here, there is a good deal of variation Pressure on the great veins may cause cyanosis and venous engorgement; this may be asymmetrical and the venous pressures in the arms may be different (10). Pressure on the recurrent laryngeal nerve may cause aphasia; on the œsophagus, dysphagia; and on the lung, dyspnœa, collapse of the left lower lobe and pleural effusion.

INTERFERENCE WITH ARTERIES. Involvement of the orifices

such as the digital. It is particularly due to exposure to cold. Some people are more prone than others, and women much more than men. The spasm of the arteriole may shut off the blood supply entirely so that the finger becomes white; or, if only a little blood is entering, the stagnation is such that all the oxygen is removed and the finger looks blue. Lewis (3) showed that the spasm was independent of nervous influences, and due to the reaction of the muscular coats of the arteries to the low surrounding temperature. It is, in fact, a local disorder of the vascular system (4) After a time intimal proliferation may interfere permanently with the circulation through the affected arteries. Another suggestion has been that there may also be vasodilatation of the palmar area which shunts some of the blood from the branches (5). But the vasoconstriction of the digitals is obviously the important point.

Since the original description of Raynaud in 1862 which did not clearly differentiate them, the name has been given to a variety of quite distinct conditions. Local asphyxia, which may be followed by gangrene, may result from thromboangeitis obliterans; from senile arterial obliteration, syphilitic arteritis, and occasionally from the syndrome associated with cervical rib Hunt (1) describes the phenomenon in ten different conditions:

A. Occurring alone.
  1. Normal persons on prolonged exposure to cold.
  2. Hereditary cold fingers.
  3 True Raynaud's disease.
  4. Local trauma, such as vibration.

B.
  5 Sclerodactylia (Acrosclerosis), after prolonged ischæmia for years

C. In the course of the distinct diseases given above.
  6. Thromboangeitis obliterans.
  7. Arteriosclerosis.
  8. Syphilitic arteritis.
  9 "Rheumatic" arteritis.
  10. Cervical rib.
  11. Some miscellaneous conditions, such as scleroderma, lupus erythematosus, polycythæmia, tubercle.

There is usually less fall in blood pressure. A sudden embolism at the aortic bifurcation might cause the symptoms in the legs, but the pain would be exclusively crural.

The "silent case," which has healed is most likely to be confused with a syphilitic aortitis, if the lesion is confined to the arch, and there is aortic reflux; and a negative Wassermann reaction will not exclude. The *sudden* development of serious incapacity and a new murmur may suggest the diagnosis (22).

TREATMENT. Absolute rest, and morphia in full doses may provide a chance of healing, and recovery may be greater than the desperate nature of the case may at first suggest.

REFERENCES

1 SHENNAN (1934) *Medical Research Council, Series No* 193
2 ERDHEIM (1929) *Virchow Arch f path Anat*, **273**, 454
3 SARTOR (1942) *Arch Path*, **33**, 704
4 HOWARD, BAYLEY (1940) *Amer Heart J*, **20**, 223
5 DAVIS (1941) *Brit Heart J* **3**, 166,
6 ROBERTS (1939) *Amer Heart J*, **18**, 188
7 GARDNER, GALBRAITH, HARDWICK (1939) *Lancet*, **2**, 1019
8 FLAXMAN (1942) *Amer Heart J*, **24**, 654
9 HAMBURGER, FERRIS (1938) *Amer Heart J*, **16**, 1
10 CLAIBORNE, HOLLER (1938) *Amer Heart J*, **15**, 358
11 BLACKFORD, SMITH (1937) *J Amer med Ass*, **109**, 262
12 GLENDY, CASTLEMAN, WHITE (1937) *Amer Heart J*, **15** 358
13 THOMAS, GARBER (1943) *Amer Heart J*, **25**, 407
14. LOGUE (1943) *Amer J med Sci*, **206**, 54
15 WAINWRIGHT (1944) *Brit Heart J* **75**, 81
16 BAYLEY, MONTE (1943) *Amer Heart J*, **25** 262
17 GOULEY, ANDERSON (1940) *Ann intern Med*, **14** 978
18. BOURNE, MILLS (1946) *Brit Heart J*, **8** 181
19 ROESLER, GIFFORD, BETES (1937) *Amer Heart J*, **12**, 650
20 EAST (1939) *Lancet*, **2**, 1017
21. MCGEACHY, PAULLIN (1937) *J Amer med Ass*, **108**, 1690
22 PERRY (1942) *Arch intern Med*, **70**, 689
23 HOSKIN, GARDNER (1946) *Brit Heart J*, **8**, 141
24 CASSIDY, PINNIGER (1946) *Brit Heart J*, **8**, 130
25 MORGAN JONES, LANGLEY (1946) *Brit Heart J*, **8**, 191
26 CAMPBELL (1946) *Brit Heart J*, **8**, 200

Raynaud's Phenomenon

"De l'asphyxie locale, et de la gangréne symmétrique des extrémités" (Raynaud 1862)

More recently this state has been well defined as "attacks of 'dead' fingers or toes, brought on by cold, without obliteration of the pulse, or massive gangrene" (1). Another definition is "*intermittent* spasm of the digital arteries, with or without local nutritional changes" (2). There is active closure of the arteries,

of the underlying tissues; with great stiffness. Similar changes may be seen in the skin of the face and elsewhere on the body. Probably the use of the term "acrosclerosis" would better define the condition when restricted to the fingers, and "scleroderma" where it is diffuse. The vascular changes associated with this condition are described elsewhere (p. 105). The Raynaud phenomenon may be conspicuous in scleroderma and dermatomyositis. In acrosclerosis pain is very troublesome. Finally the finger shrinks and nutritional changes become severe. In about three-quarters of these patients there is localised scleroderma of the face (1).

How far an acrosclerosis leads to digital-vascular obliteration, or how far ischæmic spasm is the primary cause, is undecided. We can suppose that the sclerotic changes ultimately become the dominant factor. Lewis found pathological changes in the digital arteries.

Finally, as arterial sclerosis and thromboangeitis are dealt with fully elsewhere, a word may be said about *syphilitic arteritis*. These cases exhibit the Raynaud phenomenon; there is paroxysmal hæmoglobinuria, and changes in the ears and nose are frequent. The incidence is usually among younger patients. The Wasserman reaction is positive.

"Rheumatic" Arteritis (Hunt) is said to be marked by the Raynaud syndrome arising after sore throat.

CERVICAL RIB SYNDROME. It is important to recognise this because of the possibility of relief (8). A cervical rib may damage the wall of the subclavian artery. There is compression by the rib against the scalene muscle or the clavicle. In some cases the artery and vein may be compressed between the clavicle and the first rib. The differential diagnosis may be made by paralysing the scalenus anticus with local anæsthetic (9). Inclining the head to the affected side relieves the pain. Bracing back the shoulders may provoke the attack. Interference with the brachial plexus may cause wasting of the smaller hand muscles; there is pain on carrying weights. A skiagram clinches the diagnosis of cervical rib. Raynaud's phenomenon may be seen in the fingers.

Treatment. Drugs are not really effective. Papaverine (½ grain) given [illegible]

actical (10).

A suitable

1. It is the usual physiological reaction, if the exposure be prolonged enough and severe enough.

2. HEREDITARY "DEAD" FINGERS. Far the commonest type is found under "*hereditary cold fingers.*" This reaction is probably present in some degree in 20 per cent of persons (6). The affection is usually trivial, males are affected as often as females; and the onset is usually in childhood; several members of a family are often subject to it. All grades of attack may be experienced Often the distribution is asymmetrical. Patients must avoid exposure to cold which causes the spasm, by wearing suitable clothing and so forth. As often as not this is a counsel of perfection, and the disability or inconvenience is not severe enough to warrant renunciation of pleasure, or the acceptance of tiresome restrictions and habits; or else the manual routine makes it impossible to avoid some degree of exposure. Drugs are probably of little avail. Hyperthyroidism will certainly relieve it.

3. True *Raynaud's Disease* is probably rare But some writers have certainly included many of the severer cases of Group 2. Here the onset is later, women are almost exclusively affected; the course is severe with progress towards grave disability and nutritional changes, leading to superficial necrosis and sometimes gangrene. The resulting scarring becomes very troublesome. Occasionally lesions of the nose and ears and cheeks result, as well as in the fingers and toes

Whether this is a true distinction between this condition and the milder and commoner one of dead fingers is as yet unsettled. The incidence of age and onset and the course suggests that the two are different. On the other hand, the clinical picture seems to give no line of distinction

VIBRATION. An interesting type is met with in workmen who handle vibrating tools, such as riveters and pneumatic drills (7) But here, too, the exposure to cold is the more important cause, whether from the exhaust or the cold metal, rather than the actual vibration.

5. SCLERODACTYLIA, OR ACROSCLEROSIS. Cases can be graded in degree of severity in an unbroken series from trifling transient ischæmia on prolonged exposure to cold, to the severe and persistent changes of sclerodactylia, with much pain and disability. Here the skin becomes thick and wizened, and there is thickening

tion is brought on by exposure to cold. When the hand is warmed the circulation returns and the skin becomes red and warm. Severe chilblains are common. Gangrene does not occur. The pulsation in the arteries is normal, for nothing is revealed by the oscillometer. On warming, the temperature of the skin rises in the usual way, so there is no impairment of vasodilatation.

Microscopical examination shows spasm of the smaller arterioles, with dilated capillaries.

The condition may be akin to the Raynaud syndrome. Sympathectomy, however, gives some relief, so there may be an increase in vasomotor tone, in addition to some intrinsic sensitivity to low temperature (2). Cutaneous injection of 1/1000 histamine gives a wheal in this condition, but not in Raynaud's disease. Lewis (4) concludes that in these cases there is an unusual degree of susceptibility of the small arterioles of the skin to cold. In the minor grades it is a common ailment borne by many people. It is most important to keep the hands and feet warm, by wearing suitable coverings, adequate shoes, and woollen stockings instead of silk, with gaiters in cold weather.

Telford (5) has found that preganglionic section of the white rami of the upper second and third thoracic nerves will provide relief It may be well worth while if intractable chilblains persist and cause much misery.

REFERENCES

1 [illegible] .6 175
[illegible] Clin., 15, 601.
[illegible] Heart J., 21, 780
[illegible] London

Erythrocyanosis

This is a reddish-blue discolouration of the skin in young women, affecting the legs from above the ankles upwards. It is very rare in males. The skin is purplish and cold. The minute vessels are dilated, and the arterioles are constricted [illegible] There may [illegible] form a swol[illegible] and pigmen[illegible] nodules can be felt. Itching may be severe. The nodules may break down and form ulcers. Pain may be intense, and a considerable degree of disability result.

climate may occasionally provide the solution if the patient is lucky. Otherwise avoidance of manual work that causes exposure, and suitable clothing for hands, legs and feet must be worn when the temperature is low.

If these measures are not effectual, and trophic changes are setting in, with interference with the use of the hands and much pain, sympathectomy must be considered. By this means the normal vasomotor tone is eliminated and so this degree of hindrance to maximal circulation of blood is removed. Preganglionic sympathectomy, or ganglionectomy, including D_2, for the arm, relieves, but the underlying abnormality in the vessel wall, its undue sensibility to cold, remains. The grade of relief is probably related to the grade of abnormality present before operation. Attacks are less severe and less easily provoked at first (11). The resulting degree of vasodilatation soon tends to decrease. For the most part in these cases the operation will be done to relieve the hands. Actually, the results of operation for the disease affecting the legs are better. It is important that the patient should realise that a Horner's syndrome will result, and the hands will become very dry. Bilateral lumbar sympathectomy, including L_2, may cause sterility in males.

REFERENCES

1 Hunt (1936) *Quart J Med*, **5**, 399
2 Lewis T (1936) Vascular Disorders of the Limbs London
3 Lewis T (1929) *Heart* **15** 7
4 Hyndman Wolkin (1942) *Amer Heart J* **23**, 535
5 Johnson (1941) *Surg Gyn Obst* **72** 887
6 Lewis, T Pickering (1933-4) *Clin Sci* **1**, 327
7 Hunt (1937) *Proc Roy Soc Med*, **30** 171
8 Holling (1940) *Guy's Hosp Rep* **89** 285
9 Falconer, Weddell (1943) *Lancet* **2** 539
10 Mulinos *et al* (1939) *Amer J med Sci* **197**, 793
11 Lewis T (1938) *Clin Sci* **3**, 321

Acrocyanosis

This is a functional vascular disorder affecting mainly young women. The blueness of the extremities of the limbs is usually bilateral and symmetrical. As a rule the fingers are affected, and the disturbance reaches as far as the wrists. The ears and nose may also be affected.

There is very little change in the appearance of the skin on changing the posture of the limb (1). There is no pain. The condi-

lowers the threshold of the pain nerve endings to tension and to heat. Such pain was found in patients with erythrocyanosis, thrombo-angeitis and senile gangrene. Tension was the chief cause, as the temperature of the foot did not rise. Tenderness was present and friction could provoke pain.

These cases are not true erythromelalgia, although the painful sensations are similar to those complained of in that disease. Lewis (6) has suggested that the name should be changed and "Erythralgia" substituted (redness and pain). Another term "Erythermalgia," referring to the warmth, has also been suggested (3)

REFFERENCES

1 Brown [illegible]
2 [illegible]
3 [illegible]
4 [illegible]
5 [illegible]
6 LEWIS, T. (1936) Vascular Disorders of the Limbs

Arteriovenous Aneurysm

Locally there is pain, and perhaps disability depending on the site. There may be throbbing. Pulsation, a thrill and a murmur are the cardinal signs, with some enlargement of the veins. The interesting points are the changes which occur in the circulation as a result of the arteriovenous fistula (1).

If the communication develops in a limb before the epiphyses unite there is likely to be hypertrophy. The artery proximal to the fistula shows atrophy of the middle coats; further on it is small and the pulse weak. The *veins distal to* the opening become greatly enlarged and tortuous. The oxygen content of the venous blood is increased (2)

Hæmodynamics. There is an increase in the cardiac output; there is an increase in the blood volume (3). The arterial pressure tends to fall, and the pulse rate to rise. The work of the heart is considerably increased, perhaps 25 per cent. The venous pressure tends to rise in the later stages. The heart becomes enlarged. Later, the systolic pressure tends to rise and the diastolic to fall. In the final phases there is definite congestive heart failure. Temporary closure slows the pulse and raises the diastolic pressure.

The disease is found in patients with fat legs; in fact, the patients tend to be obese and florid. Thin legs are not affected (1). It is probable that a deficient venous return, with vasoconstriction from exposure to cold in a fat limb, are the important causes. A subcutaneous inflammatory reaction then results. A parallel may be drawn to similar conditions seen in limbs affected by anterior poliomyelitis. Good results have been obtained from bilateral lumbar ganglionectomy in severe cases. Mild cases may respond to protection from cold. As Lewis remarked, the disease came in with short skirts and silk stockings, and it will go out with them.

REFERENCE

1 TELFORD, SIMMONS (1936) *Brit Med J*, 1, 629

Erythromelalgia

This very rare disease, consisting of a "painful redness of the limbs," was described by Weir Mitchell in 1878. Since then the term has been used rather loosely for several different conditions. When the feet are dependent they become very painful and hot, so that the pressure of the shoes is intolerable and walking almost impossible. When the legs are raised the pain is relieved. The pain is burning in character and of a peculiarly intolerable intensity. The foot becomes red and the pulse is full and bounding. One observer (1) found that during the attack the temperature of the skin rose. The hands might be affected. Elevation of the limb or cold relieved the pain. The rise in temperature has been confirmed (2). The critical level lies between 32° and 36°C. There is free inflow of the blood, for the oxygen content in the venous blood leaving the part is high. The small vessels appear to be deficient in tone and are distended by hydrostatic pressure (3). Under the capillary microscope it can be seen that the capillaries are enlarged and increased in number (4). The disease may occur in association with polycythæmia. Some relief to the pain may be afforded by aspirin (2). Inhalations of adrenalin are reported to be effective (3).

The ætiology of "burning" pain was investigated by Lewis (5). Pain was provoked by warming, cooling, or friction, and stretching of the skin. An inflammatory process may be associated with this sort of pain. The tissues are then in a susceptible state; and they are stimulated by some substance released in them which

REFERENCES

[illegible] Aneurysm New York.
5
J, 28, 133.
J, 33, 151
rg, 13, 357.
18, 589
Hosp, 76, 93.
Clin Sci, 5, 249

Thrombophlebitis

Venous thrombosis may result from inflammation, injury, or stasis, from certain abnormal conditions of the blood, such as after hæmorrhage, in polycythæmia, and after such infections as pneumonia and typhoid fever.

Superficial Phlebitis. This usually occurs in a superficial varicose vein, and is due to an abnormal condition of the intima aided by stasis, and perhaps trauma. The thrombosed vein is sore and tender, and the skin over it reddened. Gout is sometimes a cause. There is no danger of embolism.

Thrombosis in a previously normal vein is quite a different matter. The thrombosis is due to infection, and a septic embolus is likely to become detached. There may be soreness along the saphenous vein in the calf or thigh, for example. A small reddened patch of cellulitis can be seen and a slight brawny swelling felt. It is important to insist on rest in bed to avoid the risk of embolism, from two to four weeks.

Thrombosis of Deep Veins. Thrombosis due to injury is seen after fractures. Deep thrombosis of femoral or pelvic veins comes after abdominal and pelvic operations. Fractures of the femur with the prolonged immobilisation of the part favour the development and extension of the thrombus up to the iliac veins. Earlier mobilisation and getting up after operation should reduce the likelihood of occurrence.

Thrombophlebitis of deep veins in the leg may cause very gross œdema, which never completely clears up

Primary Thrombosis of the Axilliary Vein. It seems likely that compression of the subclavian vein by the clavicle against the first rib and subclavius muscle is a cause. Bodily build may favour this compression in some people. It occurs when the clavicle is moved backward (1). In one group of cases it is a

Pulmonary Lesions. An interesting variety of arteriovenous communication, of congenital origin, has been described in the lungs. The complaint is dyspnœa, cyanosis and giddiness. Polycythæmia may be quite high (4). There may be clubbing of the fingers. There are physical signs of a mass in the lungs, and over it there is a localised but continuous rushing murmur. The skiagram shows a shadow in one lung which spreads out from the foot and may resemble a bunch of grapes. Calcification may be present (5). The vital capacity is reduced. There may be an increase in the blood volume, up to 50 per cent (6) An intravenous injection of 70 per cent diodrast gives a diagnostic outline. Many small aneurysms may be present (7). Pneumonectomy has successfully cured some of these cases, but both lungs may be affected.

When the arteriovenous opening is closed all the abnormalities disappear Ligation of the vessels introduces little danger of gangrene as the collateral circulation is so good It would appear *that ligation and excision of the artery and vein gives the best* results. But the surgical method must depend on local factors (8).

A somewhat similar state of affairs occurs in a patient with Paget's disease (osteitis deformans), who may have congestive failure. In one such case the cardiac output was greatly raised, as also was the pressure in the right auricle The pulse pressure was high The cause was the enormously increased flow in the vascular bones It was estimated that the flow of blood in the bones was twenty times the normal. The vascularity of the *affected* bones *produced results comparable to an arteriovenous* aneurysm (9).

Klippel-Trénaunay Syndrome. The notable point is the overgrowth of one limb, or all one side of the body (hemihypertrophy). This is due to enlargement of arteries and veins; the former amounting to cirsoid aneurysms, and the latter to gross varicosity, almost angeiomatous in character. There is also superficial nævous capillary dilatation There is probably free communication between arteries and veins. Thrills and murmurs are detectable. *There is œdema and gross varicose ulceration* as a rule. The bones show increase of vascularity in the skiagram.

The cause appears to be congenital abnormalities in all types of blood vessel. Clinically it amounts to an arteriovenous aneurysm.

On account of the fairly high incidence of dangerous or fatal embolism after postoperative thrombosis, ligation of the femoral vein (7) may be combined with the use of heparin and dicoumarol.

Unfortunately it is often the case that the dangerous and fatal clots are those which form in the pelvis, and whose presence is quite unsuspected until the disaster has occurred. It has been pointed out that a source of dangerous thrombi, which form at or soon after operation may be found in the veins of the calf. Pressure may [illegible] table, or afterwards in bed. [illegible] An indefinite pain under the c[illegible] welling and thickening, a little cyanosis of the foot are easily overlooked These clots are more dangerous than those of the femoral vein extending up to Pouparts ligament (8).

How far these anticoagulants will check recurrences of the migrating type of thrombosis is not yet certain. There have been some disappointments, but there seems to be an accumulating weight of evidence that post-operative thrombosis can be controlled by these means, and the risk and incidence of pulmonary embolism lowered.

REFERENCES

1 SAMPSON (1943) *Amer Heart J*, 25, 311
[illegible]
[illegible] *Eng J Med*, 224, 139.

complication of heart failure. This may give rise to embolism. In some patients there may be malignant disease within the thorax (2). Some cases occur in healthy young men. It often comes on after exercise, such as rowing. In many cases trauma, often slight and forgotten, seems to have been the cause. The arm and hand become swollen and cold, and the superficial veins are dilated, showing a collateral circulation. The œdema does not always pit, so there is probably lymphatic obstruction as well as venous. The lesion is more common in the right arm than the left. This does not apply to left-handed persons (3). Recovery is usually complete. Embolism is unlikely (2).

Thrombophlebitis Migrans. Phlebitis of superficial veins, and also of deep, sometimes occurs in recurrent attacks. *Occasionally there is pulmonary embolism, which may be the first symptom. In other cases there is cerebral thrombosis Males are usually affected The condition may be associated with thromboangeitis* It has been held to indicate latent cancer of the stomach.

RESULTS OF PHLEBITIS. The obstruction to the vein raises the venous pressure distal to the block This leads to increased outpouring of fluid into the tissue spaces, and the formation of œdema. There is probably also some degree of venospasm, and also reflex arterial spasm, which reduces the inflow. This is not always present, as sometimes the affected limb is the warmer. Anoxæmia will further damage the capillary walls if it is present. There is also slowing up of the lymph flow. When the acute phase has subsided, arterial spasm goes. The resulting œdema may be pitting or hard and non-pitting The vein may then start to recanalise, and collateral veins will open up The limb should be elevated to aid the venous flow. *The foot should be flexed and* dorsiflexed from time to time.

Anticoagulants. *Heparin and Dicoumarol* have been extensively used *in order to prevent the extension of the thrombotic process (see p. 213).*

There is usually quick relief of the pain in the thrombosed limb (5).

In view of the chronic and recurrent course of some cases of phlebitis, it may be advisable to continue the treatment for three or four weeks. Dicoumarol should not be used where there is varicose ulceration (6).

On account of the fairly high incidence of dangerous or fatal embolism after postoperative thrombosis, ligation of the femoral vein (7) may be combined with the use of heparin and dicoumarol.

Unfortunately it is often the case that the dangerous and fatal clots are those which form in the pelvis, and whose presence is quite unsuspected until the disaster has occurred. It has been pointed out that a source of dangerous thrombi, which form at or soon after operation may be found in the veins of the calf. Pressure may initiate the trouble, on the operating table, or afterwards in bed. The local signs may be very slight. An indefinite pain under the calf, with slight tenderness, some swelling and thickening, a little cyanosis of the foot are easily overlooked. These clots are more dangerous than those of the femoral vein extending up to Pouparts ligament (8)

How far these anticoagulants will check recurrences of the migrating type of thrombosis is not yet certain. There have been some disappointments, but there seems to be an accumulating weight of evidence that post-operative thrombosis can be controlled by these means, and the risk and incidence of pulmonary embolism lowered.

REFERENCES

1 SAMPSON (1943) *Amer Heart J*, 25, 311
2 VEAL, HUSSEY (1943) *Amer. Heart J*, 25, 335
3 PELNER, COHN (1942) *Amer J med Sci*, 203, 340
4 VEAL, HUSSEY (1942) *Amer. Heart J* 23, 390
5. ZUCKER (1944) *J Amer med Ass*, 124, 217.
6 BATSON, STEWART (1942) *J Amer med Ass*, 120, 1025
7 FINE, *et al* (1942) *Ann Surg*, 116, 574.
8 HOMANS (1941) *New Eng J Med*, 224, 130

complication of heart failure. This may give rise to embolism. In some patients there may be malignant disease within the thorax (2). Some cases occur in healthy young men. It often comes on after exercise, such as rowing. In many cases trauma, often slight and forgotten, seems to have been the cause. The arm and hand become swollen and cold, and the superficial veins are dilated, showing a collateral circulation. The œdema does not always pit, so there is probably lymphatic obstruction as well as venous. The lesion is more common in the right arm than the left. This does not apply to left-handed persons (3). Recovery is usually complete. Embolism is unlikely (2).

Thrombophlebitis Migrans. *Phlebitis of superficial veins, and also of deep, sometimes occurs in recurrent attacks.* Occasionally there is pulmonary embolism, which may be the first symptom. In other cases there is cerebral thrombosis. Males are usually affected. The condition may be associated with thromboangeitis. It has been held to indicate latent cancer of the stomach.

Results of Phlebitis. The obstruction to the vein raises the venous pressure distal to the block. This leads to increased outpouring of fluid into the tissue spaces, and the formation of œdema. There is probably also some degree of venospasm, and also reflex arterial spasm, which reduces the inflow. This is not always present, as sometimes the affected limb is the warmer. Anoxæmia will further damage the capillary walls if it is present. There is also slowing up of the lymph flow. When the acute phase has subsided, arterial spasm goes. The resulting œdema may be pitting or hard and non-pitting. The vein may then start to recanalise, and collateral veins will open up. The limb should be elevated to aid the venous flow. The foot should be flexed and dorsiflexed from time to time.

Anticoagulants. *Heparin* and *Dicoumarol* have been extensively used in order to prevent the extension of the thrombotic process (see p. 213).

There is usually quick relief of the pain in the thrombosed limb (5).

In view of the chronic and recurrent course of some cases of phlebitis, it may be advisable to continue the treatment for three or four weeks. Dicoumarol should not be used where there is varicose ulceration (6).

of the heart are weak. There may be slight cyanosis of the finger nails and ears. The eyes may be sunken and the eyeballs flaccid, if dehydration is severe. The output of urine falls, almost to anuria.

Ætiology. It may be convenient to give a list of the possible causes underlying the pathogenesis. One can then consider the main physiological derangements which are present (1).

1. Neurogenic. *Derangement of the vasomotor centres* by nociceptive stimuli predominating in "primary shock." Vasoconstriction is the initial reaction.

2. Hæmatogenic. Loss of fluid from the circulation predominates here. (1) *Severe hæmorrhage* due to trauma may have occurred, whether by open loss, or as a result of the local damage associated with gross skeletal trauma. (2) *Burns* may have been extensive, causing profuse loss of plasma. (3) *Hydraulic*. In some cases dehydration may be important. Loss of fluid by severe diarrhœa, as in cholera, polyuria in diabetes, and persistent vomiting, may be important causes of depletion of the fluid in circulation. Profuse sweating is another cause of the loss of much fluid.

3. Toxic or Vasogenic. Severe toxæmia in some infections paralyses the vasomotor system and may affect the vessels directly, as in diphtheria, pneumonia and peritonitis.

To summarise, the result of these causes is that there is a discrepancy between the blood volume and the size of the vascular system. The result is a deficient supply of blood to the organs of the body (1).

Wound Shock. It is in cases of trauma, so common of recent years, that the hæmodynamics of peripheral circulatory failure have been most extensively investigated, briefly named "wound shock." The main subjects for observation are: (1) the blood volume (2) th

W

pr [illegible] the rate of the pulse, and the level of the blood pressure, and the filling of the veins, and the state of the vessels of the skin should be noted.

Decrease in the Blood Volume. In traumatic shock there is a reduction in the blood volume. This is usually the direct result of loss of blood through bleeding (2). In some conditions, such as burns and crushing injuries, the loss is chiefly of the plasma

CHAPTER XIII

FAILURE OF THE PERIPHERAL CIRCULATION

THE casualties of the second world war have stimulated further the interest in this type of circulatory failure which originated thirty years ago, and a great deal of information has been accumulated by means of new methods of investigating the circulation. The expression "shock" is short and convenient, and is used as a synonym for peripheral circulatory failure, but it introduces an idea of violent trauma which is not necessarily a constant cause. It was first made use of to describe the state of what Cannon used to call "primary shock," in which the stunning effect of some gross injury produced a vasomotor collapse of a syncopal character. "Secondary shock" was the term used to describe the later features of peripheral circulatory failure. The word "shock" has come to stay, even if its meaning has been transferred from a name of the cause to a description of its effect, for the longer name is rather cumbersome, if more precise. It must be remembered that many causes are involved, and the duration of the state of shock, and the rate of its development, modify the clinical picture to a considerable extent. The condition is not usually static, but likely to become a progressive vicious spiral which may end in the death of the individual.

Clinical Picture. In many respects this is fairly constant, but may be modified a good deal by the degree to which certain variable factors may be present. The patient is apathetic, yet often well aware of what is going on. Sometimes there is restlessness. Pain may be severe, depending on the extent of the injuries that may be present. There is usually thirst. The aspect is pale, whether from loss of blood or vasoconstriction, and the skin generally cool, and there is often profuse sweating. There may be air hunger if deficiency of oxygen is grave. The temperature is often subnormal. The pulse weak and "thready"; usually it is fast, but the rate varies; the blood pressure tends to be low and the pulse pressure small. The cervical veins are empty and the sounds

The fall in the pulse rate and the vasodilatation are the important changes, for the actual stroke output of the heart does not tend to fall any further in these syncopal attacks (3). This sudden fall in pressure may occur after the removal of relatively small quantities of blood, as a result of an abrupt failure of the peripheral resistance (7).

Later Results. CARDIAC OUTPUT. After a large hæmorrhage, the effects are as given above. In less severe cases an adjustment is effected which reproduces the state of affairs found in severe and prolonged anæmia. Then the cardiac output actually rises, in spite of the fact that the blood volume is still low (8). How this is achieved is not clear, but some venopressor mechanism may be at work.

HÆMODILUTION. Adjustments take place in the volume of the circulating blood. Initial estimations of the degree of anæmia resulting from severe hæmorrhage are apt to be misleading. The hæmoglobin level only falls at first to 80 or 85 per cent after a loss of over two pints, so that dilution is only of the order of 15 to 20 per cent. Full dilution does not occur until some forty hours after the loss of blood (9) (7). These points introduce technical difficulties in estimating the blood volume. Insufficient mixing may occur, or dilution or loss of blood may take place during the estimation, so that samples vary.

RENAL FUNCTION. In shock, from whatever cause, the excretion of urine is very scanty. It has been shown that the rate of glomerular filtration and the flow of plasma through the kidneys is reduced (10). Thus it is evident that the low excretion is not merely due to a low blood pressure. The renal flow falls to about one-tenth of the total blood flow, although in the normal person at rest one-quarter of the total blood flow passes through the kidneys. It would appear that there is a vasoconstrictor action of the renal arterioles which may have a beneficial effect on the circulation as a whole by shunting a proportion of the cardiac output from the kidneys, or there may be some change in the circulation within the kidneys. This alteration in the renal circulation does not activate the renal pressor mechanisms. It seems likely that the demonstration of a secondary circulation in the kidney, which acts as a by-pass to the renal cortex, as the results of Trueta and his fellow workers at the

rather than of the whole blood. This point introduces certain differences which will be considered later.

CHANGES IN THE VENOUS SYSTEM. The state of oligæmia leads to the following results (3): Reduction in the volume of the circulating blood causes a decrease in the filling of the veins, so *that the return of venous blood to the heart is reduced. This* causes a fall in the output of the heart. It is possible that other factors influence the efficiency of the venous return, apart from the volume of the venous blood returning. The lack of muscle tone and minor muscle movements may aid peripheral stagnation. This *is the failure of what Yandell Henderson has called the "tonic booster* pumps" (4). The result is that clinically the veins appear empty.

CHANGES IN THE ARTERIAL CIRCULATION. Three points have to be considered here. As has been noted, the cardiac output falls. This fall in output tends to lower the arterial blood pressure. The level of the blood pressure depends on three variable factors, (1) the viscosity of the blood, which can be omitted for the moment; (2) the cardiac output, which is falling, and (3) the resistance due to the tonic contraction of the peripheral arterioles. The output can be *measured accurately by catheterisation of the* right auricle, using the Fick principle, and the blood pressure is easily ascertained. The peripheral resistance can then be gauged. It is apparent that there is a rise in the peripheral resistance, which is no doubt an attempt to maintain the blood pressure, just *as acceleration of the heart helps to maintain the minute volume.* The pallor, and evident vasoconstriction of the superficial vessels, are clinical evidence of the method whereby the peripheral resistance is increased

These are the main features of the peripheral circulatory failure which are characteristic of shock whatever the cause.

VASOVAGAL REACTIONS. McMichael (2) and Richards (5) point out that further reactions may occur These may be described as vasovagal. The acceleration of *the heart gives way to slowing,* and the blood pressure falls profoundly. This drop in pressure appears to be due to a vasodilatation in the vessels of the skeletal muscles (3). This reaction was demonstrated in the forearm muscles by the plethysmograph, and is *brought about by the* autonomic nervous system, for blocking the main nerves with local anæsthetic abolishes it (6).

The fall in the pulse rate and the vasodilatation are the important changes, for the actual stroke output of the heart does not tend to fall any further in these syncopal attacks (3). This sudden fall in pressure may occur after the removal of relatively small quantities of blood, as a result of an abrupt failure of the peripheral resistance (7).

Later Results. CARDIAC OUTPUT. After a large hæmorrhage, the effects are as given above. In less severe cases an adjustment is effected which reproduces the state of affairs found in severe and prolonged anæmia. Then the cardiac output actually rises, in spite of the fact that the blood volume is still low (8). How this is achieved is not clear, but some venopressor mechanism may be at work.

HÆMODILUTION. Adjustments take place in the volume of the circulating blood. Initial estimations of the degree of anæmia resulting from severe hæmorrhage are apt to be misleading. The hæmoglobin level only falls at first to 80 or 85 per cent after a loss of over two pints, so that dilution is only of the order of 15 to 20 per cent. Full dilution does not occur until some forty hours after the loss of blood (9) (7). These points introduce technical difficulties in estimating the blood volume. Insufficient mixing may occur, or dilution or loss of blood may take place during the estimation, so that samples vary.

RENAL FUNCTION. In shock, from whatever cause, the excretion of urine is very scanty. It has been shown that the rate of glomerular filtration and the flow of plasma through the kidneys is reduced (10). Thus it is evident that the low excretion is not merely due to a low blood pressure. The renal flow falls to about one-tenth of the total blood flow, although in the normal person at rest one-quarter of the total blood flow passes through the kidneys. It would appear that there is a vasoconstrictor action of the renal arterioles which may have a beneficial effect on the circulation as a whole by shunting a proportion of the cardiac output from the kidneys, or there may be some change in the circulation within the kidneys. This alteration in the renal circulation does not activate the renal pressor mechanisms. It seems likely that the demonstration of a secondary circulation in the kidney, which acts as a by-pass to the renal cortex, as the results of Trueta and his fellow workers

Oxford have shown, may lead to further important developments in this aspect of the local results of shock.

FINAL CHANGES. IRREVERSIBLE SHOCK. If the state of shock *is prolonged, a state of "irreversible shock" is reached, and death* occurs. This final phase can be produced in dogs by keeping the blood pressure at a low level by bleeding (11). The cause is severe and prolonged anoxia. The prolonged anoxia affects all the tissues of the body (12). Possibly the circulation to large areas of the vascular system is shut off, in the same way as that to the kidneys has been shown to be. Administration of oxygen in high concentration will *not save dogs when shock is profound and prolonged*, since the shut off areas will *get no oxygen* (13). Failure of the *tone of the peripheral arterioles may aggravate the shock so that* it becomes irreversible (14). The myocardium may be unable to respond to any increase in venous pressure produced by transfusion (14). Possibly there is also a failure in some venopressor mechanism. *There may now be atony and dilatation of the* capillaries (15). *At post mortem these appear congested*, and minute hæmorrhages are found. At the end the blood is con*centrated (1) (10)*, as *though there had been some escape of* plasma from the circulation into the tissues The question *of the possibility of increased capillary permeability has been disputed*. Using radioactive proteins combined with iodine, no evidence could be found that they escaped from the circulation at any place other than that where trauma had occurred. This conclusion only applied to post-hæmorrhagic shock (16).

A good deal more information is needed about the changing phenomena of final irreversible shock, which is in fact a process of dissolution. *Little is known about the* extent to which the higher centres in the nervous system may be involved. It is safe to say *that there is a breakdown in every vital function. Changes* in the blood chemistry are now *progressive and acidosis* develops. (5).

The Circulation in Traumatic Shock. As *we have seen, the* state of peripheral circulatory failure known as shock may be due to several causes, which may be present *alone or together*. Some of the conspicuous deficiences in the circulation already described are present with them all. But there is a good deal of *variation* in the relative degree of their intensity. Certain special features of the different types will now be reviewed and compared.

The information is based on the article by Richards (5) which describes very extensive investigations by teams of workers.

A series of cases showing shock was studied. The pressures in the arm veins and in the right auricle were measured. The arterial pressure was taken. The blood volume was estimated, as well as the plasma volume, the volume of the red cells and the amount of the plasma proteins. The cardiac output was recorded. The renal clearances were also estimated. The cases were divided into five classes.

1. Skeletal Trauma (Extensive Fractures) without Shock. Here the blood volume, venous and arterial pressures, output and peripheral resistance were all normal. It may be concluded that if skeletal trauma is not associated with a fall in blood volume shock does not occur.

2 Skeletal Trauma with Shock. The total blood volume was reduced by 35 or 40 per cent. This corresponds to a loss of about two litres, which agrees with Noble's estimate of the amount of loss needed to cause full shock (17). In these patients there is considerable loss of blood and plasma at the site of bony injury. The right auricular pressure was reduced to 70 per cent, but the pressure in the arm vein was normal or even a little high, indicating venoconstriction to be present. This is evident enough since it is the cause of the difficulty in putting needles into veins in shock. The cardiac output was diminished by over 30 per cent. There was a considerable fall in arterial blood pressure. The peripheral arteriolar resistance, calculated by the fraction

$$\frac{\text{Blood pressure}}{\text{Cardiac output per second}}$$

was actually *normal*. Thus it would appear that there was a diminution in the vascular bed caused by venoconstriction to compensate for the diminished blood volume. Hæmatocrit readings showed that there was hæmodilution, although this was insufficient to restore the volume of the blood to normal.

3. Hæmorrhage with Shock. Here the figures for blood volume, right auricular pressure and cardiac output were the same as in the cases of skeletal trauma. The average level of the blood pressure was, however, rather higher, indicating a higher degree of peripheral resistance. Here, too, hæmodilution was noted. The

hæmodilution in both these groups is presumably due to inflow of fluid derived from the tissues generally. The initial fall in blood volume is due to loss at the site of injury, and not to general loss through increase of capillary permeability. This is obvious enough in frank hæmorrhage, but may be less conspicuous when there is escape of blood and plasma into the muscles and tissue at the site of injury. A large volume of loss may not cause any conspicuous increase in the size of a limb, such as the thigh.

ABDOMINAL INJURIES WITH SHOCK. The blood volume was somewhat low in these cases, but not so low as in those with hæmorrhage. But the right auricular pressure was very low, and the cardiac output decreased. A difference from the cases with hæmorrhage lay in the presence of hæmoconcentration. Probably this was due to loss of plasma into the peritoneal cavity, for peritonitis was present The fall in the blood volume was chiefly due to the loss of the plasma.

In contrast to the cases with trauma and hæmorrhage the arterial pressure was somewhat high, indicating a higher peripheral resistance. Possibly the increased viscosity of the blood partly accounted for this. Experiments on dogs with tourniquet shock showed that a low blood pressure after trauma where much plasma was lost, was more grave than after trauma associated with hæmorrhage. Shock might be severe and the blood pressure still relatively high because of the high viscosity of the blood due to hæmoconcentration from loss of plasma (16). The low level of the auricular pressure suggests some breakdown of the mechanism controlling the venous return

BURNS WITH SHOCK. The fall in blood volume was greater than in the cases with abdominal injury. The right auricular pressure fell rather less than in the other groups. The cardiac output was diminished to about the same degree Possibly there was more compensatory venoconstriction The blood pressure was fairly well maintained, indicating a high peripheral resistance. The feature peculiar to these cases was the pronounced degree of hæmoconcentration due to the profuse loss of plasma from the burned areas. This loss appears to be proportional to the areas burned (17). The high degree of the viscosity of the blood would help to maintain the arterial pressure

These groups can be divided into two types, those with

hæmodilution, following severe skeletal injury and hæmorrhage, and those with hæmoconcentration following burns and peritoneal injuries. Injection of dyes in the latter group show that in them the loss of dye is far greater than in hæmorrhage or skeletal trauma, and confirms the gross loss of plasma (18). In one group the fluid pours in from the tissues and dilutes the blood, in the other it pours out, and leaves it concentrated.

In the cases of traumatic and hæmorrhagic shock there was anoxia of all the tissues. The oxygen content of the venous blood was low, showing that the tissues were using more oxygen than normal; restlessness might account, to some extent, for this high oxygen consumption. The saturation of the arterial blood with oxygen was normal, but the anæmia and low output meant a diminished oxygen supply. There was some degree of acidosis, the lactic acid in the blood being high; this tended to increase as the degree of shock progressed.

Study of these groups of cases has done much to clear up the basic changes in the hæmodynamics which cause failure of the peripheral circulation. Less is known about certain other types.

Toxæmic Shock. Clinically it has long been suspected that in some cases of severe infection, such as pneumonia, typhoid, diphtheria, peritonitis, some degree of peripheral failure may develop and contribute to a fatal result. In some of these there may be loss of fluid from sweating, diarrhœa or large exudates. But such evidence as there is does not indicate that there is any great fall in the blood volume (5, 19). The cardiac output falls, and so does the blood pressure, so that the patient *may be* almost pulseless. The peripheral resistance is *presumably* low. The veins are probably relaxed, for the venous pressure is not raised.

In these cases raising the venous pressure by transfusion does not lead to improvement. Probably the whole cardiovascular system is damaged and fails as a whole. An additional possibility has been suggested by *Rich* (20). In various acute infections he found areas of necrosis in the suprarenal cortex with inflammation and exudate in the deeper zones. A failure of the suprarenals might well aggravate the collapse of the circulation. To what extent toxins from damaged tissues may later aggravate shock is uncertain. As an initial cause they probably play little or no part

hæmodilution in both these groups is presumably due to inflow of fluid derived from the tissues generally. The initial fall in blood volume is due to loss at the site of injury, and not to general loss through increase of capillary permeability. This is obvious enough in frank hæmorrhage, but may be less conspicuous when there is escape of blood and plasma into the muscles and tissue at the site of injury. A large volume of loss may not cause any conspicuous increase in the size of a limb, such as the thigh.

ABDOMINAL INJURIES WITH SHOCK. The blood volume was somewhat low in these cases, but not so low as in those with hæmorrhage. *But the right auricular pressure was very low, and* the cardiac output decreased. A difference from the cases with hæmorrhage lay in the presence of hæmoconcentration. Probably this was due to loss of plasma into the peritoneal cavity, for peritonitis was present. The fall in the blood volume was chiefly due to the loss of the plasma.

In contrast to the cases with trauma and hæmorrhage the arterial pressure was somewhat high, indicating a higher peripheral resistance. Possibly the increased viscosity of the blood partly accounted for this. Experiments on dogs with tourniquet shock showed that a low blood pressure after trauma where much plasma was lost, was more grave than after trauma associated with hæmorrhage. Shock might be severe and the blood pressure still relatively high because of the high viscosity of the blood due to hæmoconcentration from loss of plasma (16). The low level of the auricular pressure suggests some breakdown of the mechanism controlling the venous return.

BURNS WITH SHOCK. The fall in blood volume was greater than in the cases with abdominal injury. The right auricular pressure fell rather less than in the other groups. The cardiac output was diminished to about the same degree. Possibly there was more compensatory venoconstriction. The blood pressure was fairly well maintained indicating a high peripheral resistance. The feature peculiar to these cases was the pronounced degree of hæmoconcentration due to the profuse loss of plasma from the burned areas. This loss appears to be proportional to the areas burned (17). The high degree of the viscosity of the blood would help to maintain the arterial pressure.

These groups can be divided into two types, those with

and the blood pressure low, it shows that there is a state of vasoconstriction attempting to compensate for a much diminished blood volume and output. If the skin is warm the prospects are better, even if the blood pressure is low, for a quick recovery may be expected. Probably the blood volume and output are not so low as in the others, and less vasoconstriction occurs (1). In many cases the clear-cut types defined by Richards cannot be distinguished and one must be prepared for "mixed" types. In some patients the deleterious vasodilator effects of alcohol add a serious complication. To evaluate the relative importance of the many and various factors which may be present, changing in their severity almost from hour to hour, requires much clinical judgment and experience.

Treatment. The sooner treatment is undertaken the quicker the recovery. It is better to anticipate the graver phases of shock than to rescue the patient from a progressive and dangerous decline into the irreversible state, when no treatment avails.

TRANSFUSION. To restore the volume of the blood to its normal level is the first consideration. Whole blood should replace loss of blood. To replace lost blood with plasma will aggravate hæmodilution. When half the blood lost is restored the blood pressure is usually satisfactory. The first pint should be given in a quarter of an hour, followed by another more slowly. If a good response is obtained, and there is no further bleeding (23), the systolic pressure should rise 10 to 20 mm. Hg per pint. To make the patient safe from relapse probably at least four pints will be needed. Loss of plasma from oozing may continue for a long time, even if frank bleeding has ceased. In cases of shock from burns plasma is adequate.

Fluids. Hot drinks, such as tea and coffee, are most useful, as there is often thirst.

Posture. The patient should lie flat, except perhaps in chest injuries. Elevation of the feet is undoubtedly of value. The blood pressure is raised, and the patient becomes more alert.

Temperature. Warming the skin is likely to be harmful, as the compensatory vasoconstriction *may* be interfered with. On the other hand, the body must not be exposed to cold.

Oxygen. Oxygen, even in high concentration, has been rather disappointing. Cases of chest injury will *need* it. In most cases the arterial oxygen saturation is normal.

Peripheral Failure in Heart Disease. Shock may be a very grave complication arising early after a coronary occlusion. In heart failure the venous pressure rises; while in shock the right auricular pressure is low. After coronary occlusion, it has been shown that the blood volume is normal, the output of the heart low, and the arterial pressure reduced. The right auricular pressure may be somewhat raised (5). This *would show cardiac failure.* There are some resemblances to shock in the pallor, low skin temperature, sweating and fall in blood pressure (21). It may be difficult to decide which type of failure, cardiac or peripheral, predominates. Congestion of the pulmonary circulation, causing dyspnœa, and signs of œdema of the lungs are important indications of left ventricular failure, which may reach a severe degree before the jugular vessels appear to be engorged. Even when the venous pressure rises, the output may fall, as though the heart could not respond to the increase in filling pressure.

It has been suggested that the state of shock may lead to fresh coronary occlusions, and so institute a vicious circle, owing to failure of the coronary circulation (22). In the final phases of heart failure it seems probable that failure at the periphery is present too, for the whole circulation has broken down. The visible stagnation in the vessels of the skin, the cyanosis, and chill, and failure to respond to venesection all point to this; but the original cause was primarily cardiac. More precise information is needed about shock in coronary occlusion, and much is still obscure.

Pulmonary Embolism. Shock may be severe soon after pulmonary embolism. Then the tendency to develop jugular engorgement may be counterbalanced by the tendency for the venous pressure to fall as a result of shock (see p. 153)

Clinical Observations in Shock. The elaborate measures described above are not ordinarily available for clinical observation. The rate of the pulse can be deceptive—vagal slowing may be a serious symptom if associated with vasovagal collapse. The level of the blood pressure is of the greatest value (23). In almost all cases the arterial pressure is parallel with the severity of the failure. A progressively falling pressure is always a serious sign. On the other hand there may be severe shock after burns, with but little fall in pressure. The feel of the pulse to the educated finger is very informative. If the skin of the extremities is cold and pale,

REFERENCES

[illegible] (194?) *Amer Heart J* 23 147

[illegible]

13 FINE, FRANK (1943) *J clin Invest*, 22, 304
14 WIGGERS, WERLE (1943) *Am J Physiol*, 136, 421
15 WIGGERS (1941) *Ann intern Med*, 15, 178
16 FINE, SELIGMAN (1944) *J clin Invest*, 23, 731
17 NOBLE (1946) *J clin Invest* 25, 172
[illegible]

Morphia should be given in doses large enough to control pain or restlessness.

Vasoconstrictor Drugs. Methedrine (20 mg. by intravenous injection or 30 mg. intramuscularly) seems to be helpful in vasovagal collapse (3). The use of suprarenal extracts is still in the experimental stage. Paredrine (10-20 mg. by intramuscular injection) causes venoconstriction and so might be useful (24)

Except to combat failing vasomotor tone the use of vasoconstrictors at present is limited; but in vasovagal crises they may be valuable, and there are distinct possibilities of drug therapy, especially with regard to the induction of venoconstriction.

Salts of Sodium. As considerable amounts of sodium are lost by various channels, particularly in burns, it seems logical to replace it. There is some evidence that sodium chloride aided recovery from shock due to burns in rats (25). Large doses of sodium bicarbonate (50 grammes in 48 hours) taken by mouth, cause slight increase in venous pressure and plasma volume in normal persons, and so might be useful in peripheral failure (26). They would combat the tendency to increasing acidosis in cases who are doing badly.

Liver has been found to be useful in reducing the mortality and increasing the survival time after burn shock in mice (27) This might be valuable in human beings

In view of the large amount of *protein* lost, the intravenous replacement should be supplemented by protein by mouth as soon as possible. *Alcohol* should never be given as it is a vasodilator. *Coramine* and *strychnine* do not touch the basal abnormalities in most cases, but perhaps stimulate failing medullary centres *Digitalis* is valueless, and indeed harmful.

Although recent investigations have thrown much light on the hæmodynamics of peripheral circulatory failure, much is still obscure. Modern methods are needed to elucidate the peripheral failure in the acute infections, in such states as diabetic coma and Addison's disease. It is still unknown why the sudden vasovagal breakdowns occur, or why some cases pass into irreversible shock; nor are all the features of this fatal condition as yet understood.

When peripheral failure complicates infection, treatment of the infection must be the first aim. Penicillin and the sulphonamides have altered the whole outlook here. When fever is high, hydrotherapy in the form of tepid sponging is beneficial.

lead from the right arm, is —3 mm., and T in VL —2 mm., lead I will be —2 —(—3) = +1 mm. This is the reason for the positive T found sometimes in lead I in anterior infarction. In lead III the polarity is such that a relative state of positivity at the left leg is represented by an upward movement of the fibre. To obtain the deflections in lead III, VL must be subtracted algebraically from VF (the left leg unipolar lead). Lead II is the sum of leads I and III.

The chest leads CR and CF are also bipolar leads, but differ in that the effect of the remote electrode is much less than that of the chest electrode, since the latter is so much nearer the heart. The potentials at the chest are between three and five times greater than those at an extremity (1), so that the influence of the extremity electrode is only about a quarter that of the chest electrode. But in chest leads knowledge is sought only of the potentials over the precordium, and any effect at all from the remote electrode will distort the curve.

Einthoven Triangle Hypothesis. In 1913 Einthoven, Fahr and de Waart enunciated their hypothesis that, having regard to the comparatively great distance to the extremities, the heart could be regarded as being at the centre of an equilateral triangle formed by the two wrists and the left ankle, and that therefore the algebraic sum of the potentials at the three points of the triangle at any given moment in the cardiac cycle was zero for all forces parallel to the plane of the triangle. This hypothesis has been accepted by nearly all the leading experimenting cardiologists since that time If then the three limbs are connected to a central *terminal* which is used as the remote electrode, all forces parallel to this plane will be eliminated, and the remote electrode, to that extent, will be indifferent. It is recognised that the cardiac vector moves in three dimensions and *not in two*, but the forces involved in the perpendicular movement are considered to be small, and not to exceed 0 3 mv (1) Thus it is claimed that the potential of the central terminal never exceeds *±0.3* mv throughout the cardiac cycle, and that for practical purposes these leads can be considered to be unipolar. Wilson (2) named the leads when the central terminal was used, "V" (voltage) leads.

Wilson (1) interc...
terminals tc
with and \

CHAPTER XIV

NEW THEORIES ABOUT CARDIOGRAMS

SOME NEW POINTS IN THE THEORY AND PRACTICE OF CARDIOGRAPHY

In this chapter there are two important topics for discussion; in the first place the technique and theory of unipolar leads is considered. After that there is consideration of some new points of view which seek to elucidate the physical changes upon which the cardiogram depends. *No doubt one should be able to give an* electrical explanation for every deflection in the curve, and there is no question that much has been achieved in this respect. Most important of all and of chief value to the clinician is the more accurate localisation and diagnosis of pathological change.

Unipolar Leads

The standard leads are bipolar *They represent the difference* in potential between the two points at which contact is made. In lead I the electrodes on the two wrists are connected, and the galvanometer records the difference in potential between them. The instrument is set—or speaking technically, the polarity is such—that a state of relative positivity at the left arm is represented by an upward movement of the fibre. To obtain the *difference in potential between the two arms*, which is recorded by the galvanometer, the voltage at the right arm must be subtracted algebraically from that at the left. Thus, if the size of the deflection T is − 2 mm. at the right arm, which equals −0.2 millevolts, and +1 mm. at the left arm, T in lead I will be +3 mm. Therefore, *since the potentials at the right arm are usually negative* except in extreme right or left axis deviation, it will follow that T in lead I will often be more positive than in lead VL, the left arm unipolar lead. If the potentials at both arms are negative, but the right arm is more negative than the left, the deflections in lead I will be positive. That is to say, *if T in VR, the unipolar*

appreciable only in about 10 per cent of cases. The deflections in VR are uniformly negative, giving a positive error in CR leads, except in extremes of left or right axis deviation when the deflections are small or diphasic, and the error is then negligible. In VF leads the deflections are small and positive when the electrical axis is normal; with moderate left axis deviation (semi-horizontal heart) they are so small as to cause no error. With increasing left axis deviation, they are negative but still small, giving a small positive error. In right axis deviation (vertical heart), however, the T deflections tend to be large and positive with the result that a considerable negative error may be present in CF leads involving the risk in some cases of recording a negative T which is due to distortion

Unilateral Ventricular Hypertrophy. The diagnosis of preponderating unilateral ventricular hypertrophy by means of multiple chest leads is based on the following principles. Active heart muscle is electrically negative to inactive muscle. The impulse spreads down the Purkinje tissue in the sub-endocardial zone, and reaches the ventricular cavities almost at once, which are therefore negative throughout the QRS phase. The impulse then spreads outward through the ventricular muscle: as it does so, the muscle which has been activated will be negative, while in front of the advancing wave there will be a zone of positivity. This is reflected to the surface of the body and causes a positive wave (R) to be the first major deflection to be recorded in health When the impulse finally reaches the epicardium a state of negativity is reflected to the surface of the body and a downward negative deflection then takes place This deflection is called the "intrinsic deflection" (Lewis). The prolongation of this deflection into an S wave depends on whether that part of the ventricular muscle over which the electrode lies has been activated early or late in the cardiac cycle. By the time that the impulse has reached the surface of the right ventricle, the left ventricle will not yet be fully activated. The right ventricle will then become negative to the left and an S wave will be inscribed in leads over the right of the precordium Should, however, the electrode be over the thickest part of the left ventricle, the whole heart will be in systole when the impulse has reached the epicardium in that region. The QRS phase will be over; no current flows and the fibre

apparatus consists of three limb terminals which are brought together at a central terminal. To this is attached the right arm terminal from the cardiograph, the left arm terminal being employed in the usual way for the exploring electrode.

Unipolar Limb Leads. With the unipolar technique the potentials at any point on the surface of the body can be ascertained. Unipolar limb leads were formerly obtained by attaching the exploring electrode to the limb to be examined as well as the terminal for the remote electrode, but the deflections were often very small. Goldberger (3) showed that deflections of the same shape but of 50 per cent greater magnitude resulted when the exploring electrode was substituted for the remote electrode terminal on the limb to be examined. To obtain the right arm potentials by this method the exploring electrode is attached to the right arm, and a "V" connection is attached to the left arm and left leg, the third being allowed to hang loose. Unipolar limb leads are termed VR, VL and VF. Goldberger proposed that his leads should be termed "augmented unipolar limb leads" (a VR, etc.), but with the general adoption of the method the "a" (for augmented) has been dropped.

Distortion from CR and CF Leads. *It has recently been suggested that the differences between CR, CF and V leads are so slight as to be negligible* (4); and that therefore CR leads (5) or CF leads (6) are to be preferred. The probable distortion in CR leads can be predicted from the measurements of the deflections in lead VR; and in CF leads from the deflections in lead VF. In each case the figures of these measurements must be divided by about six if the augmented method of Goldberger is used, since the extremity electrode only exerts about one quarter the influence of the chest electrode and the Goldberger method magnifies the deflections by a third ($\frac{1}{4}\times\frac{2}{3}=\frac{1}{6}$). *The result must be subtracted* algebraically from the figures for the measurements of the chest leads in order to obtain the true potentials. Thus negative potentials in lead VR will result in a positive error in CR leads for subtracting a negative means adding a positive. Examination of 300 VR and VF leads has showed that the T deflections were 3 mm. or less in 88 per cent of the cases in VR leads, and in about VF leads (7). This would give a distortion

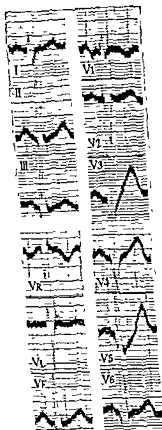


FIG 89
Right-sided hypertrophy in a girl of ten with mitral stenosis and active rheumatism S is almost absent in V1 The heart is vertical

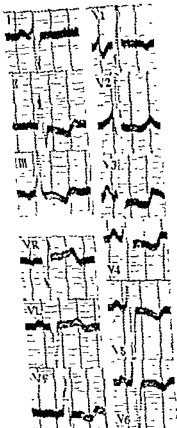


FIG 90
Right ventricular hypertrophy from a case of atrial septal defect Note large late R in lead V1 and predominant S waves appearing in V4, V5 and V6 T is inverted in V3, V4, V5 and V6 This was due to digitalis The heart is vertical.

the S waves deepen. As a minimum requirement the size of the R waves should be less than one quarter of the magnitude of the S waves which should exceed 12 mm (7) The transitional point swings over to V4 and V5. The R waves may be large in V4 and V5. In advanced cases T is inverted in V4, V5 or V6 and the QRS is widened. These changes are not affected by rotation of the heart (Fig. 88).

comes to rest at zero potential; the S wave is consequently absent.

In normal subjects, using the six positions for the chest electrode, it will be found that the voltage of R is about half that of S in V1 and V2 and that they are equal in magnitude at about V3 which is situated approximately over the interventricular septum. S is absent or diminutive in V5 or V6 (Fig. 87). In left ventricular hypertrophy the R waves become diminutive in V1 or V2 and

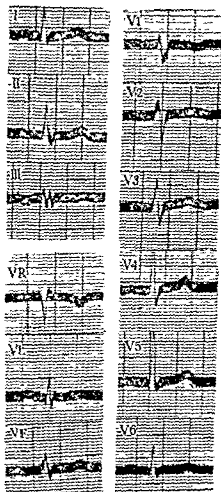


Fig. 87

Normal chest leads and unipolar limb leads. R is half the voltage of S in V1 and V2. S almost disappears in V5 and V6. The transitional point is between V2 and V3.

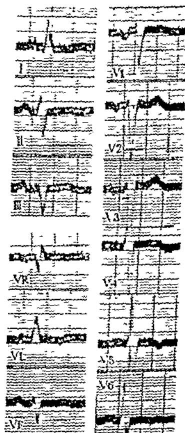


Fig. 88

Left ventricular hypertrophy. Chest leads show diminutive R waves with deep S waves in V1, V2 and V3; transitional point between V4 and V5; increased size of complexes; inversion of T in V5 and V6. QRS 0.10 second. The heart is horizontal.

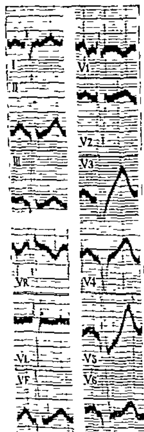


Fig 89
Right sided hypertrophy in a girl of ten with mitral stenosis and active rheumatism S is almost absent in V1 The heart is vertical

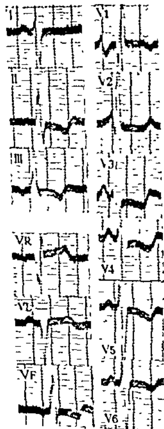


Fig 90
Right ventricular hypertrophy from a case of atrial septal defect Note large late R in lead V1 and predominant S waves appearing in V4, V5 and V6. T is inverted in V3, V4, V5 and V6 This was due to digitalis The heart is vertical

the S waves deepen. As a minimum requirement the size of the R waves *should* be less than one quarter of the magnitude of the S waves which should exceed 12 mm. (7) The transitional point swings over to V4 and V5. The R waves may be large in V4 and V5. In advanced cases T is inverted in V4, V5 or V6 and the QRS is widened. These changes are not affected by rotation of the heart (Fig. 88)

In right ventricular hypertrophy a large and late R, sometimes preceded by a Q, occurs in V1, S being absent. T is usually inverted. The late R may be seen only in V1 (Fig. 89) but sometimes also in V2 and V3 (Fig. 90). S waves appear in leads further to the left, but there is no abrupt transitional point. Considerable hypertrophy of the right side is needed to cause these changes since the right ventricle must approximate in thickness to the left.

Occasionally the late R wave may be seen in a lead midway between the right border of the sternum and the right midclavicular line (V3R) when the usual chest lead series is normal (8).

Unipolar Limb Leads and the Position of the Heart. When the heart is in a normal position the openings of the aorta and pulmonary arteries and to some extent of the pulmonary veins point upwards and to the right. A lead entering the chest at the right shoulder will face these vessels and through them the ventricular cavities. Although the deflections of the right arm lead are not the same as those obtained with an intra-cardiac electrode, since adjacent structures have some effect, they are similar. The ventricular cavities are negative throughout almost the whole of systole, and the deflections of the right arm lead are also negative unless the heart is very much rotated. If the heart is rotated clockwise, becoming more vertical, the great vessels will tend to point directly upwards, or midway between the two shoulders. In that case the deflections of the left arm lead will take on the same characteristics as those of VR and become negative (Figs 89, 90). A vertical heart may be caused by a low left diaphragm, as in narrow slender chests or emphysema, or by right ventricular hypertrophy. When the heart becomes more horizontal, rotating anti-clockwise about an antero-posterior axis, as occurs in left ventricular hypertrophy or with a high left diaphragm, lead VF has negative complexes (Fig. 88).

There are two possible explanations for this Wilson (1) considers that when the heart is horizontal the aorta and pulmonary arteries issue horizontally, or midway between the right shoulder and the diaphragm, and so lead VF, which enters the chest through the left diaphragm, so to speak, takes on some of the characteristics of lead VR and has inverted complexes. Goldberger (9), however, points out that the zone of positivity which lies in front of the advancing head of the impulse as it spread through each

ventricle is equalled by a zone of negativity at the tail of the wave. In health lead VF will face each ventricle equally. It will therefore face the advancing head of the impulse and the initial deflection will be positive. If the heart is vertical, lead VF will face more of the left ventricle, and the initial deflection will be more positive still. When the heart lies horizontally, lead VF will face more of the right ventricle; but it also faces the tail of the wave in the left ventricle, which in that position lies superiorly. The left ventricular muscle mass is greater than that of the right ventricle and exerts a larger potential, and so the stronger state of negativity of the tail of the wave in the left ventricle will overcome the smaller positive potential of the advancing wave in the right ventricle and a small negative initial deflection will be found. In this view an S wave in the left leg lead always signifies that the heart is horizontal.

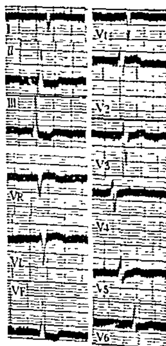


FIG 91.
Rheumatic mitral disease with hypertension, and auricular fibrillation Standard leads show right axis deviation, but R in V1 and V2 is diminutive and S in V2 is deep indicating left ventricular hypertrophy The heart is vertical

Bilateral Ventricular Hypertrophy. By means of the combined use of a chest lead series and unipolar limb leads, a diagnosis of bilateral ventricular hypertrophy can often be made The chest leads will show left ventricular hypertrophy, while the unipolar limb leads will show that the heart is vertical. Standard leads often show right axis deviation (Fig 91). Unless the chest is very emphysematous a vertical heart in the presence of left ventricular hypertrophy is always due to secondary hypertrophy of the right side.

Bundle Branch Block. In bundle branch block the affected side receives the impulse through the septum from the healthy side. The ventricular cavity on the diseased

side will be positive during the early phase of the QRS, and the negative intrinsic deflection over it will be late in the QRS. In left branch block the intrinsic deflection in leads over the right side occurs early in the QRS, and the R wave is diminutive. It *may* be absent in V1 if the heart is horizontal since, when the great vessels issue horizontally, a lead to the right of the sternum *may* have some of the characteristics of the right arm lead. In leads over the left ventricle the intrinsic deflection is delayed in the QRS and there is *no* S wave. In right branch block the opposite is seen. A wide R with no S occurs in lead V1, the downward limb of the R constituting the intrinsic deflection, and being late in the QRS. In leads to the left an R occurs, but its downstroke is comparatively early and is followed by a wide S during which the right ventricle is activated. Owing to the greater thickness of the left ventricular wall, the intrinsic deflection does not occur as early as in leads over the right ventricle in left branch block, but the R wave is slender.

When the heart is in a horizontal position, lead VL reflects the potentials over the left ventricle and has positive deflections. Lead VF in that position usually has smaller negative deflections, resembling those of VR. Lead I is VL – VR, whilst lead III is VF – VL. The deflections of VL will therefore be reversed in these two leads, being positive in lead I and negative in lead III. This is the reason for the discordant curves seen often in left bundle branch block with positive deflections in lead I and negative deflections in lead III (page 249).

It is in right branch block that the two explanations for the direction of the complexes in lead VF lead to divergent results. Wilson (1) considers that if lead VF has complexes resembling those of the leads over the left side of the precordium and the complexes of lead VL resemble those on the right side of the precordium, the heart is placed vertically (Fig 51). In Goldberger's explanation an S wave in lead VF always means that the heart is horizontal. In right branch block a deep S is frequently present in lead VF and in leads V5 and V6 over the left of the precordium. This, according to Wilson, would mean that the heart is vertical, while according to Goldberger it is horizontal. In such cases we have seen concomitant hypertension and the heart enlarged to the left *on screening* so that the explanation of Goldberger would seem to be preferable

REFERENCES

1 WILSON *et al* (1944) *Amer Heart J*, 27, 19
2 WILSON *et al* (1934) *Amer Heart J*, 9, 447.
3 GOLDBERGER (1942) *Amer Heart J*, 24, 378
4 GEIGER, GOERNER (1946). *Amer Heart J*, 32, 163
5 HOYOS, TOMAYO (1947) *Amer Heart J*, 33, 698
6 WALLACE, GROSSMAN (1946) *Brit Heart J*, 8, 83
7 BAIN, REDFERN To be published.
8 MYERS, KLEIN, STOFER (1948) *Amer Heart J*, 35, 1
9 GOLDBERGER (1944). *Amer Heart J*., 28, 621

Some New Theories about Electrocardiograms

During the last few years a good deal of attention has been directed to the elucidation of the electrical changes in the heart muscle which underlie the QRS-T deflections. Some doubt has been thrown on the validity of the theory on which the conception of Einthoven's triangle hypothesis is based, but it still remains sound. The matter is extremely technical and needs a fuller equipment in the knowledge of mathematics and physics than the ordinary cardiologist can boast. It seems desirable to attempt a short and simple survey of some of the articles on the subject. One of the most useful applications of this study seems to throw light on the pathogenesis of the curves of infarction. (The introduction of multiple unipolar praecordial leads has been valuable in helping to elucidate some of these problems.) It will be, perhaps, most useful to readers to start by recalling what occurs in a single isolated cell of muscle when it becomes active.

In its resting electrical state the heart muscle cell is to be regarded as a mass of living protoplasm enclosed in a semi-permeable membrane The positive cations can pass through this membrane and range themselves on its outer surface. The negative anions cannot pass through, and range themselves on its inner surface. The cell is now polarised, and the twin charges, positive and negative, are called "doublets" Using expressions from electrical physics the negative charges may be called "sinks," and the positive charges "sources" When the cell is stimulated at one side by an impulse, the surrounding membrane at that spot becomes permeable and the anions can pass out. Depolarisation thus begins at the stimulated end. Electrical equilibrium is upset, and a current will flow from the end which is still polarised back to the depolarised end, if one were to imagine that the two ends were connected by a conductor to form a circuit. The current will flow

until the state of depolarisation is complete throughout the cell. As soon as this state is reached the cell is in a condition of uniform electrical activity. When this is over the process of repolarisation will begin at the end where depolarisation started. This will cause a current to flow back through the imaginary conductor in the direction opposite to that of the current of depolarisation. This current will cease when the electrical "doublets" are restored and the state of polarisation is once more complete. If a galvanometer were included in the circuit its indicator would record a diphasic movement, the first phase quick and the second slow, for the phase of activation is fast, and that of recovery gradual.

Ventricular Activation. The ventricular myocardium is a syncytium. It is provided with the Purkinje system which conducts the impulse stimulating activity as fast as possible over the inner surface of the ventricular cavities. An appreciable interval of time elapses, however, between the activation of the parts near the lower end of the septum, which receive the impulse first, and the parts which receive it last, in the upper part of the conus arteriosus and the upper and outer part of the wall of the left ventricle. Here it arrives 0 03 second later Purkinje tissue conducts the impulse ten times as fast as heart muscle fibre, so the passage of the impulse through the ventricular wall is relatively slow

As the process of activation spreads over the inside of the ventricular cavities, the electrical charge on the inner surface becomes negative to that on the outer pericardial surface, which is positive. There is then a difference of potential across the ventricular wall which persists until the impulse reaches the pericardial surface, which then becomes negative too

Vectors. In electrical matters the term "Vector" is used to denote any quantity that has "magnitude", "sense," which may be positive or negative; and "direction." A vector can thus be drawn as a line, whose length is proportional to its magnitude and whose direction shows its position in space. The point in space from which it originates is called its "origin" the point in space to which it is directed is called its "terminus" The "sense" of the vector can be indicated by the plus or minus sign.

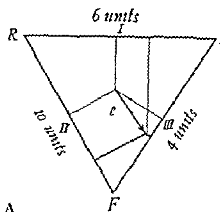
As activation progresses within a ventricle, what is termed a "shell" of electronegative potential is set up within the cavity.

Across a polarised surface, on one side of which the negative

anions are ranged, and on the other the positive cations, the vector points at right angles, from the negative to the positive side. When dealing with the hollow electrical "shell" lining the ventricle, the vector of electromotive force of the ventricle will be at right angles to the plane of the opening of the margins of the shell. The length of the vector will be proportional to the area of the opening of the shell. The direction of the vector of the right ventricle at any given moment of time will be different from that of the left for anatomical reasons. The two vectors can, however, be summated by translating them to a common point of origin, without altering the sense or magnitude or direction of either. By drawing the parallelogram of forces, of which they will form two sides, its diagonal will give the sum or resultant of the two vectors. In this way the two vectors of the two ventricles can be added. The line of the diagonal gives the magnitude and direction of what has been called the electrical axis of the heart. Lewis long ago pointed out that the spread of the impulse in the right ventricle was clockwise in direction, and anti-clockwise in the left ventricle.

The "termini" of serial positions of the vector *of the right* ventricle during activation will therefore describe a different path in space from that of the left for the general direction of the *spread* of the impulse is different on the two sides The *record of the* movement of the terminus of a vector is called the *vector cardiogram* The electrocardiograph records the potentials of the *sum of* the vectors of the two ventricles. While the QRS complex is being written the direction of the cardiac vector or electrical axis is constantly changing. It is possible to determine the direction of the vector at any given moment *of time if* the standard leads are recorded simultaneously, or if *corresponding* points are considered on each lead, when taken *separately in* the usual way. The direction of the vector can be found by *using* Einthoven's triangle (Fig 92A) It can also be plotted *on the* "triaxial reference system" where the three sides of the triangle are drawn through a central point at angles *of* 60° to each other, and marking off six sectors, according to Bayley's method (1) (Fig. 92B).

Hill (2) shows that if unipolar limb lead



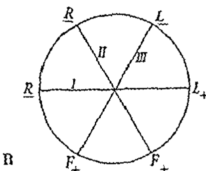


FIG 92

The three leads are drawn through a central point The relative potentials at their ends are shown + or — (After Bayley)

This difference can be reconciled by introducing a factor $\sqrt{3}$. For the mathematical proof of this the article should be consulted.

PLOTTING THE VECTOR. By plotting the height, in millimetres for choice, of corresponding deflections in two leads, say I and III, on the appropriate sides of Einthoven's triangle, so that one end of the segment is at the centre of the side, and the other marked off along the side according to whether its value is plus or minus, two points are obtained from which perpendiculars (normals) can be drawn. One normal from the centre of each side will pass through the centre of the triangle the other two will intersect, and give the point from which the line may be drawn to the centre of the triangle, which will give the position projected on the frontal plane of the electrical axis, or indicate the magnitude and direction, at that given moment, of the cardiac vector (Fig. 92A).

In this figure, 6 positive units of length, say millimetres, are measured along the side of the triangle corresponding to lead I. Four units are similarly measured, positive, along lead III, and the intersection of the "normals" from the ends of these sections gives the position and length of the vector e, which is the electrical axis at that moment. The vector e subtends a section of 10 units of length on lead II, which is the sum of 4 and 6.

The same procedure can be conveniently adopted in Fig. 92A, in the Bayley method; by marking out the appropriate lengths, positive or negative, along leads I and III from the centre, and dropping intersecting perpendiculars at the end of each section marked off.

In a normal heart, normally placed in the chest, it can be shown that the vector resulting from the sum of the two vectors in both ventricles rotates during the phase of activation in an anti-clockwise direction: the article by Gardberg and Ashman (3) should be consulted for a very clear exposition of these ideas.

The Vector Cardiogram. The first important work on this subject was done by Schellong and others in 1937 (4). Latterly the technique has been taken up by Wilson and Johnston (5).

The vector cardiogram can be recorded in this ingenious way. By using a cathode ray tube the luminous spot on the fluorescent screen can be made to record the electromotive force of the heart beat. By means of suitable connections the movements of the luminous spot will correspond to the movements of the terminus of the cardiac vector. The isoelectric point of the spot corresponds with the central point of Einthoven's equilateral triangle *or* of Bayley's triaxial reference system. During the inscription of QRS the spot will describe a loop, or elongated oval, and may be written either by clockwise or anti-clockwise movement. The first records were collated with the QRS deflections. It was shown that the vector cardiogram could be written in two planes, using frontal and anteroposterior contacts. Its spatial *projection could* then be demonstrated. The loops could be viewed stereoscopically (4). The loop was collated with the QRS (6) and it was thought that it might be useful in distinguishing notching and splintering of pathological origin from that of no account (7) The convention is to describe the clockwise loop as "positive," and the anti-clockwise as 'negative" In a normal person the long axis of the positive loop lay at an angle of about +60° to the horizontal (Fig 93); it will be remembered this is the angle which E (the electrical axis) forms with lead I. In a case of left axis deviation a "negative" loop was described, and the lie of the angle of the axis of the loop to the hori-

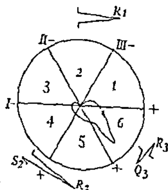


Fig 93

Normal loop, showing relationship between QRS loop, and the normal ECG deflections on the

zontal was about − 50°; in another case it was −20°. In right axis deviation the "positive" or clockwise described loop showed an angle of +150° to the horizontal at its maximum. By projecting the loop on the sides of an equilateral triangle it is possible to draw the QRS for each lead; the position of the spot of light in its circuit being used to show at which moment of time corresponds to which wave of QRS.

This correlation of older data by quite novel means is of considerable interest.

Howard (8) points out that the V.C. (vector cardiogram) is, in fact, a space curve, for the body's field extends in three dimensions. The V.C. as written is then a projection on the frontal plane in two dimensions, just as the E.C.G. is derived from potential differences recorded in the frontal plane. By means of a fairly simple geometrical method, based on the triaxial reference system, in which, as we have seen, the three sides of the Einthoven equilateral triangle are drawn through one central point, Howard shows how the vector cardiogram can be constructed by measuring the size of the deflections, positive and negative, in each of the three standard leads. The "loop" for the T-wave can also be plotted. For details the original article must be consulted. The curves those plotted agree very well with those plotted by the cathode ray oscillograph.

It is found that a positive clockwise loop is the normal for nearly all hearts normally placed in the chest, both for QRS and for T. In left axis deviation the loop is negative (anti-clockwise). There is some evidence to show that myocardial disease may reverse the rotation of the loop for QRS, while the T loop remains unchanged. The further application of this method of analysing the cardiogram will be interesting.

The Ventricular Gradient. It has been shown that in properly standardized curves, when the height of any given deflection in lead I is added to the height of the same deflection in lead III, the sum gives the height of that deflection in lead II. This is shown in Fig. 92A These measurements only give the position of the electrical axis, or of the direction and magnitude of the cardiac vector, as projected on the frontal plane of the body at the given instant. A further possibility has been explored whereby the element of time can be introduced. During the phase of activation

(or depolarization), the direction of the vector or electrical axis is constantly changing, but it is possible to arrive at its average position throughout that time. The same applies to the phase of repolarization. The two may also be considered together.

Wilson, Macleod and Barker (9) showed that if the *areas* enclosed by the QRS deflection were measured by a planimeter, the area of QRS_1, plus area of QRS_2=Area of QRS_2. These areas are measured in terms of time and voltage, so they actually represent microvolt-seconds. If these areas are substituted for the figures of the amplitude of the deflections on the sides of Einthoven's triangle they give the inclination of the electrical axis during the *whole* of the QRS interval, which is called the "mean electrical axis." The "mean electrical axis" of T can be found in the same way, by measuring the area enclosed by the T waves and plotting the result on the Einthoven triangle. As Wilson and others (10) point out, the mean electrical axis of QRS gives the direction, in the plane of the Einthoven triangle, in which the process of depolarisation spreads The mean electrical axis of T gives the the direction of the spread of repolarisation. The two manifest areas, of QRS and of T can now be considered together. The *manifest* area of QRS-T is a measure of the effects due to local variations in the excitatory process. If the excitatory *process* spread and regressed uniformly throughout the muscle, the area of QRS and the area of T would be equal, and opposite in *sign, and* their sum, the area of QRS-T, would be zero. But as this is not the case, it is held, therefore, that the area of QRS-T gives the *measure* of local variations in the excitatory process, and the electrical axis of QRS-T indicates the line along which they are greatest.

If these measurements of *the areas of QRS-T* are plotted in the same way as the electrical axis, it is possible to define a vector, for it has magnitude and direction. The *name given to it is* the "ventricular gradient," sometimes indicated by the letter G.

The word "*gradient*," then, means a difference in level of electrical potential *This* difference in potential is a vector, for it has magnitude, and it also *has* direction; the two levels of potential, between which the gradient (or slope, if one might ... the word) are located ...

... the magnitude and direction ...

electromotive force formed by a lack of uniformity in the duration of the excited state in the heart muscle. The "gradient" would not exist if the sequence of repolarisation were the same as depolarisation. The ventricular gradient expresses the electrical forces which result from a difference in the sequence of repolarisation from that of depolarisation (11). Changes in the ventricular gradient reflect changes in the muscle. Changes in the T wave, apart from those of bundle branch block, which are related to a particular type of QRS, may show changes in the muscle. The familiar experiment of cooling the apex and causing T wave inversion is an example of this (12).

Changes in the Normal Human Ventricular Gradient. While it is clear that changes in the gradient as reflected in alteration in the T wave may indicate changes in the state of the myocardium, as has long been known, there are other variations to be explained which may be seen in the cardiograms of normal *hearts. It is well known that these variations may be due to* alterations in the position of the heart in the thorax. Vector analysis may now attempt an explanation of these deviations from the normal. Variation in the position of the heart in three dimensional space can be analysed by considering the possibilities of *rotation* about one or more of three axes. We must consider rotation round the anteroposterior axis, which may be described *as clockwise, to the right, to a more vertical position, or counter-*clockwise, to the left, to a more transverse position. Next there is the possibility of rotation about the longitudinal axis of the heart, clockwise or counter-clockwise, as viewed from the apex. Thirdly, rotation may occur round a transverse axis so that the apex may come to lie further forwards or further backwards in the anteroposterior plane. There may be simultaneous rotation about two or three of these axes, *particularly as regards the longitudinal* and anteroposterior.

Rotation Round the Anteroposterior and Longitudinal Axes. Just as rotation of the heart about an anteroposterior axis changes the direction of the QRS axis, so does it alter the direction of the ventricular gradient. The negative T_3 of a transversely placed heart comes to mind. The reason for this will be apparent when rotation around the *longitudinal* axis is considered. A vertical heart is rotated clockwise round its long axis,

when viewed from the apex, so that the left ventricle comes to lie even further behind. A transversely situated heart is rotated counter-clockwise round its long axis when viewed from the apex, so that the left ventricle comes to lie more to the front. Thus rotation round the anteroposterior axis is associated with rotation, clockwise or counter-clockwise, round the longitudinal axis. In fact, clockwise rotation round the anteroposterior axis is associated with clockwise rotation round the longitudinal, and vice versa. Actually we shall see that this rotation affects the relative positions in space of the three axes; the QRS, the gradient, and the anatomical or longitudinal. In a transverse heart, when viewed from the front, the gradient lies more transversely than the longitudinal axis; in a vertical heart the gradient lies more vertically than the longitudinal axis. Rotation about the longitudinal anatomical axis of the heart will then affect the position in space of the gradient. The rotation may thus be clockwise or counter-clockwise when the heart is viewed from the apex. Expressed in relation to the change in the QRS axis, after *clockwise* rotation round the long axis, the position of the gradient vector lies somewhere between 5° to the right and 35° to the left of the mean QRS axis. After *counter-clockwise* rotation the position is between 32° to the right and 10° to the left of the QRS axis

If we now consider the three axes together, the anatomical, the QRS and the gradient (QRST), the gradient vector or axis, in clockwise rotation around the anatomical longitudinal axis, when plotted, will be found to lie to the right of the long axis, and the QRS axis will be found still further to the right (Fig. 94A). If the heart is rotated counter-clockwise round the long axis, the gradient vector will be found to lie to the *left of the* anatomical long axis, and the QRS axis still further to the left (*Fig. 94B*). If the longitudinal anatomical axis points downward, forward, and to the left, the relative changes in the positions *of the QRS* vector and of the gradient vector can only be explained by supposing that the gradient axis points less far forward--*lies, in fact*, in a posterior plane, so that clockwise rotation swings it to the right. The fact that counter-clockwise rotation swings the QRS through a wider arc and brings it to the most leftward position suggests that it lies in a plane still further behind. Three pipe cleaners

are orientated in space relatively to one another as suggested above. The conclusion is that the axis of the gradient (QRS-T) in three dimensional space must lie *behind* the anatomical axis about which longitudinal rotation occurs: the QRS axis lies still further behind. Therefore in clockwise rotation about a longitudinal axis, the axis of QRS will point further to the right than that of the gradient; in counter-clockwise rotation the QRS axis will swing further round to the left and lie to the left of the axis of the gradient, describing a larger arc.

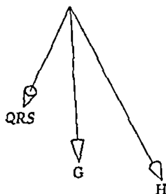


Fig 94A

Showing effect of clockwise rotation about *H* on the relative positions in space of G and QRS (After Ashman and Byer)

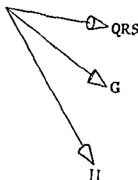


Fig 94B

The same heart as in A *Showing the effect of counter*-clockwise rotation about H, on the relative positions in space of G and QRS (After Ashman and Byer)

H Longitudinal axis of rotation of the heart
G Gradient—a vector
QRS Mean axis of QRS complex

It will be remembered that normal hearts when placed vertically in the thorax are rotated clockwise round an anteroposterior axis, while transversely placed hearts are rotated counter-clockwise. In the former (*vertical*) *lead* I *shows S and no Q*, while lead III shows Q and no S. In the latter (transverse) there is Q in lead I, and S and no Q in lead III (11). So far the direction of the axes or vectors G and QRS have been considered as projected on the frontal plane. But, as these relatively different degrees of change in the axes G and QRS on rotation about the longitudinal axis suggest, in three dimensional space, they are actually on

different planes, one behind the other, and are in fact separated, probably by an angle of 30° (12).

ROTATION ROUND THE TRANSVERSE AXIS. Since these variations in the position of the heart must be considered as taking place in three dimensional space, it remains that the third possibility of rotation round the transverse axis must be taken into account. The anatomical longitudinal axis of the heart points downwards, to the left, and forwards. In persons with deep chests, anteroposteriorly, the heart will lie with the apex pointing more forwards. When the chest is shallow from back to front, the apex will lie pointing further backwards. Thus it will come about that the angles which the axes QRS and the gradient form with the frontal plane of Einthoven's triangle will alter. An axis may, when lying more anteroposteriorly, be foreshortened in the frontal plane (cast less shadow as it were), and the converse will also hold (Fig. 95). This rotation round the transverse axis will affect both the axes of QRS and of the gradient; not necessarily to the same extent in each case, and so be the cause of unusual degrees of deviation in their spatial relationship. In the cardiograms these variations in position will be reflected by differences in QRS and T, which may appear without relationship to one another.

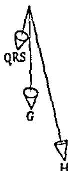


FIG 95
Showing a vertical heart rotated backwards around its transverse axis, and the foreshortening effect on QRS, and to a lesser degree on G (After Ashman and Byer)

Abnormal Changes in the Ventricular Gradient. Changes in the manifest magnitude of the human ventricular gradient (QRS-T axis) may be due to several causes. An increase in rate diminishes the magnitude of the gradient, and vice versa. The flattening of T in tachycardia is familiar enough. Change in posture from supine to erect may cause an extreme decrease. It may be that change in rate and decrease in stroke volume are the underlying factors in ordinary cardiograms. Various changes in T have long been known to occur, on alteration in rate and sometimes in posture This new approach may help to elucidate these alterations in T when studied from the viewpoint of the magnitude and direction of the vectors represented by the ...

areas of QRS and QRS-T (12). Since it appears that in three dimensional space the axis of the QRS vector points backwards relative to the axis of the gradient (QRS-T) vector, the angle between them cannot be truly reflected on the frontal plane. Rotation round the long axis of the heart and perhaps about its transverse axis will materially affect the position in space of these axes, both to one another and relatively to the anatomical long axis of the heart itself. These apparent discrepancies between the anatomical axis and that of the mean QRS axis have led to questions as to the validity of the method of Einthoven's triangle for plotting the position of the vectors (13). It may be possible to account for them when they are considered in this way.

It may be that when the deviation between the axes of QRS and QRS-T (the gradient) is greater than would be expected after due allowance has been made for the possible effects of rotation about the longitudinal and transverse axes, the cause is likely to be some abnormal state in the myocardium. On purely empirical grounds there are fairly definite conclusions as to the significance of changes in the T wave in many instances. Studies on these lines will place such ideas on a firmer foundation; even if vector analysis be too elaborate and time consuming for ordinary clinical work, the results obtained should be easily applied.

Deviations of the RST segment can be explained in the absence of gross myocardial injury or pericarditis. They are, in a sense, physiological rather than pathological. They are due to variations in the repolarisation of the muscle. The deviation is opposite in direction to the main QRS deflection. It is suggested that repolarisation of the subendocardial surface is in advance of the depolarisation of the epicardial surface. The RST deviations due to digitalis appear to be caused by changes in the repolarisation curve. In left ventricular hypertrophy a type of what might be called T wave deviations may be seen. They are opposite to the main deflection. In order to distinguish the physiological type of RST deviation from the pathological, such as are seen in infarcts, the names "repolarisation" or "regressive" deviation and "injury" deviation have been suggested (14).

Interpretation of the Effects of Injury and Ischæmia or Myocardial Infarction on the Cardiogram

The important paper of Bayley (16) deals with this subject. As a result of occlusion of a coronary artery some of the muscle dies. Outside the dead zone there is a zone of injury, and outside this a zone of ischæmia, adjacent to the healthy muscle. The injured zone produces a current of injury, for during diastole a positive potential (source) is directed towards the healthy muscle and a negative potential (sink) towards the dead. In taking the curve this injury current is neutralised by the compensating current introduced into the circuit. The current of injury in diastole may be represented by a vector pointing to the centre of the chamber affected, and lying at right angles to the plane of the surface of the infarct. But as accession of activity means some reversal of polarisation, a current will flow again and cause the displacement of the RS-T junction (p. 197). As the injured zone gradually disappears, by death or recovery, so the injury current diminishes (1). The T wave changes which remain are due to the persistence of an ischæmic zone in which the onset of repolarisation is abnormally slow during diastole.

Another suggestion is that potential differences arise as a result of blocking at the edge of the injured tissue of the wave of excitation. If a unipolar electrode is placed over an infarct it will record a *positive* RS-T deviation, for the spot is positive to the negative and active muscle near by.

The modern theories of the interpretation of electrocardiograms have been applied by Bayley (16) in an attempt to elucidate certain curves which indicate myocardial disease. Much of the matter is too extensive for short survey *here*; it is concerned with electrophysical theory, and with a mathematical analysis; it is well worth careful study. But it may be possible to give some indication of some interesting explanations which account for the well-known changes in the cardiogram from myocardial infarction

An infarct is a dead, electrically inert region in the wall of the ventricle. The electrical axis of *the* heart in three dimensional space may be regarded as a vector, which is the sum of two components; these are the two vectors, one representing th

electrical charges of accession which occur during activation of the *right ventricle, and the other of those which occur in the left.* This cardiac vector is recorded as projected on the two dimensional frontal plane of the body. The movements of the terminus of the cardiac vector describe a loop during which the QRS is written. This loop is the vector cardiogram, and may be recorded by a suitable apparatus, the cathode ray tube, as has been described. An electrically inert zone occurring in the wall of a ventricle interferes with the uniform spread of accession (or the building up of the electrical shell on that particular side). It will be clear that actually the dead zone really gives rise in a sense to electrical forces because the differences in potentials in the diametrically opposite part of the affected ventricle are now unopposed. These *are negative to the relatively positive potential of the dead area's inner surface. During the phase of accession an electromotive* force develops round the dead region. If the electrically positive surface of this area is directed towards the centre of the ventricle, the vector due to this force will be directed at right angles to the plane of the centre of the area in which it is generated, in fact from the centre of the dead zone to the centre of the ventricle The length of the vector (representing its magnitude) will depend on the area of the dead zone

In the case of a posterior left ventricular infarct, its vector will be directed upwards, forwards and to the left. From this position *in three dimensional space it will be projected on to the two* dimensional frontal plane when the record is taken.

If this vector be projected on to the "triaxial reference system" of Bayley (in which the three sides of Einthoven's equilateral triangle pass at their centres through a central point, thus forming 6 sextants, numbered from 1, at three o'clock, round anti-clockwise to 6 at four-thirty o'clock); the initial loop of the vector cardiogram will be distorted into the first sextant. This will produce a positive deflection, R, in lead I, a negative deflection (Q_2) in lead II, and a negative deflection in lead III (Q_3) (Fig. 96).

One may infer, as already *stated, that the size of the* Q_2 and Q_3 will depend on the area of the dead surface that gave rise to them. If the infarct is very small, and surrounded by healthy muscle, it may *produce* no effect at all.

Similarly this reasoning may be applied to anterior infarcts.

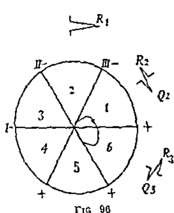


FIG 96
Loop displaced by posterior infarct
(After Bayley)

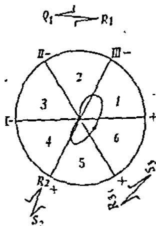


FIG 97.
Loop displaced by anterior infarct (After Bayley)

The positive inner surface will be directed downwards, backwards, and rather to the right. The vector, at right angles to the centre of this plane, when projected on the triaxial reference system will distort the initial phases of the QRS "loop" into the fourth or fifth sextant There will then be a small Q_1, and initial R_2 and R_3 (Fig. 97)

If an infarct were perfectly anterior, so that the vector of its electromotive force were exactly at right angles to the frontal plane, it is clear that this force could exert no influence on the QRS, for it would have no projection (cast no shadow, as it were, with the sun directly overhead). In this way the changes in the initial phases of QRS may be worked out for infarcts in any position It is clear that in the case of two diametrically opposed similar infarcts, one would theoretically neutralize the effect that the other might produce

This is then a very brief exposition of the basis of the theory of changes in the initial deflections in QRS as effected by infarcts according to their site and size. But not only do these dead areas affect the electrical changes of the process of accession, they also affect the process of regression, as shown by changes in the T wave.

The order of regression in the ventricles is determined by the order of accession. Thus to some degree QRS determines the form

of T (as in bundle branch block). But local lack of uniformity in the duration of the excited state will modify T. The order of regression will then be changed from its usual relationship to the order of accession (QRS).

As we have seen, by measuring the *areas* of QRS in two (or three) leads, results can be obtained, which when plotted on the triangle of Einthoven, or the corresponding triaxial reference plane, define a vector for the whole duration of QRS, not for one instantaneous moment. This vector quantity is a measure of the *total* magnitude of the electrical effect during QRS, and its direction shows the *average* direction of the accession wave during this time.

Similarly, a vector can be plotted by using measurements of the T waves. It will show the magnitude and average direction of the electrical forces of *regression*. To recapitulate some of what has already been said, we may decry that if the vector of accession were equal and opposite to that of regression, their sum would be zero—they would cancel out. But in the normal cardiogram this is obviously not the case. The normal order of regression is not the same as that of accession. There is lack of uniformity in the changes in the ventricular muscle wall, at the endocardial and epicardial surfaces. This lack of uniformity can be expressed by adding the vectors of accession and regression to form a new vector, the gradient, called $\hat{G}$. (It may be noted that a circumflex denotes a vector quantity.)

$$(\hat{A}\ QRS + \hat{A}\ T = G)$$

where $\hat{A}$ QRS indicates the vector derived from the *area* of QRS and $\hat{A}$ T the vector derived from the *area* of T. This third vector derived from QRS-T is the mean electrical axis of QRS-T, and is called, as we have seen, the "ventricular gradient" Its magnitude depends on the effect of the total lack of uniformity during systole, its direction must lie along the line where these variations are greatest.

By measuring these areas of QRS-T in the standard leads the direction of the vector (gradient) can be plotted in the frontal plane of the triaxial reference system (or of Einthoven's triangle) But actually, as we have seen, it lies in three dimensional space (as do the others). When A denotes a vector depending on the areas of QRS and T respectively

$$\text{If} \quad \hat{A}\ QRS + \hat{A}\ T = \hat{G}$$
$$\text{then}\ \hat{A}\ T = \hat{G} - \hat{A}\ QRS$$

In fact, the area of T will depend on the area of QRS and the gradient. What alters QRS may alter T, causing secondary T wave changes. What alters the gradient will alter T, and "primary" T wave changes are the result.

An example of a "secondary" T wave change is that seen in bundle branch block; of a "primary" T wave change is that due to digitalis.

The lack of uniformity in the regression phase is held by Bayley to be local and to exist at the epicardial and endocardial surfaces of the ventricular muscle. The normal gradient vector has a base to apex direction, pointing from those areas where the duration of activity is longest to those where it is shortest. If the gradient also points rather backwards, as already shown, in three dimensional space, one would infer that the areas of longest lasting activity were antero-basal surface areas, and those of the shortest duration in the postero-apical region.

Bayley points out that ventricular ischæmia, acute or chronic, is the most important cause of alteration in the position of the gradient in space, and consequently of its projection on the frontal plane. This alteration, reflected as a primary change in the T wave, is determined by the intensity and site of the ischæmia in the ventricular wall. The endocardial surface has a better chance of maintaining its blood supply than the epicardial. The position of the normal QRS-T vector or gradient is affected by this ischæmic zone, and it tends to be drawn into a line at right angles to the centre of th[illegible]

[illegible] must change with A G. In the case of posterior infarction $\hat{A}$ T will pass into the second sextant of the triaxial reference system, and project a negative T wave in leads II and III (Fig. 98).

Similarly, in anterior infarction $\hat{A}$ T will be found in the fifth sextant, projecting a *negative* T wave in lead I (dotted line) (Fig. 98).

If local [illegible]

jury

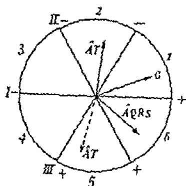


FIG 98.

(After Bayley)

At the edge of a dead area there is a zone of injury. During diastole there will be a difference of potential at *this place*; the *positive* or "source" surface will be directed towards the normal, the "sink" or *negative towards the dead muscle.* We have seen how this difference of *potential may constitute the current* of *injury*. This current *may cause* the RS-T deviation (the Pardee curve) of myocardial infarction.

Bayley explains the evolution of the cardiographic changes associated with infarction in the *following* way. Ischæmia of muscle is the *initial* effect of impaired coronary flow. This abnormal state in the muscle causes primary changes in the T wave or *gradient*. If the *blood supply becomes worse, an injured zone* develops *within* the ischæmic zone. If this injured zone reaches the epicardial surface the injury current from it causes displacement of the RS-T junction. Most of the *primary* T *wave* change then disappears. If the flow is re-established these minor RS-T junction displacements *may go* But if an infarct develops, as shown clinically by fever, leucocytosis, increase in B.S R., the injured zone extends so *that* the outer ischæmic zone becomes small. The centre of the *injured zone* dies. The *maximal RS-T* junction displacements *now* develop and with them abnormalities in QRS as well, of which the appearance of Q is the most *signifi-cant, showing a transmural infarct* [illegible] epicardial [illegible] and [illegible]

D[illegible] the injured zone diminishes, for *some* of it recovers to the ischæmic state and some dies completely. It *may* now no *longer* be in contact with the [illegible] and [illegible] [illegible] were seen, come back and may persist.

Summary. The development of the abnormalities in the cardiogram may be based on the following fundamental phases.

To begin with, as the result of ischæmia the gradient is diverted, and this causes the primary and temporary alterations in the T wave. There is, in fact, a local change in the lack of uniformity of the excited state. With the development of a zone of injury a current of injury is formed. This may be represented by a vector whose direction is at right angles to the plane of injury, pointing towards the centre of the ventricle, and whose length is proportional to the area of the plane of injury. This vector will divert the QRS vector; the result will be RS-T junction deviations and alterations in QRS, particularly the development of Q waves if the infarct is transmural; at the same time the primary T changes vanish. As healing progresses the injury current fades, with disappearance of junction displacements in R S-T; the gradient diversions reappear as negative T waves, for an ischæmic zone is present again; the QRS changes may partially regress. Next, the secondary T wave changes may disappear finally. But there may remain a permanent diversion of the vectors of QRS and T, which persist as permanent abnormalities in QRS and permanent secondary abnormalities in T. If the infarct heals up, and remains embedded in normal muscle, without surrounding ischæmia, the curve will *resume a normal* appearance.

Bayley and Monte (17) report an interesting case in whom they recorded changes in the T wave of the type they consider to be caused by ischæmia. Analysis of QRS-T areas showed that the direction of the gradient vector had rotated in an anti-clockwise direction. This "negative" rotation is held to be associated with posterior infarction. Actually postmortem examination showed that ischæmia of the posterior part of the left ventricle had occurred from obstruction to the right coronary artery by a dissecting aneurysm Sections of the heart muscle in this area showed no pathological change. They consider that the ischæmic state may last for a considerable time—perhaps for two weeks—indicated by T wave changes, without cardiac pain and without pathological change. We have recently followed transient T_1 changes, lasting some weeks in a case which showed no ischæmic changes in the front of the left ventricle at autopsy.

Experiments by Bayley and La Due (18) have shown that in dogs complete occlusion of a coronary artery, causing ischæmia,

FIG 98

(After Bayley)

At the edge of a dead area there is a zone of injury. During *diastole* there will be a difference of potential at this place; the positive or "source" surface will be directed towards the normal, the "sink" or negative towards the dead muscle. We have seen how this difference of potential may constitute the current of injury. This current may cause the RS-T deviation (the Pardee curve) of myocardial infarction.

Bayley explains the evolution of the cardiographic changes associated with infarction in the following way. Ischæmia of muscle is the initial effect of impaired coronary flow. This abnormal state in the muscle causes primary changes in the T wave or *gradient*. If the blood supply becomes worse, *an injured zone develops within the ischæmic zone. If this injured zone reaches the epicardial surface the injury current from it causes displacement of the RS-T junction.* Most of the primary T wave change *then* disappears. If the flow is re-established these minor RS-T junction displacements may go But if an infarct develops, as shown clinically by fever, leucocytosis, increase in B S.R., the injured zone extends so that the outer ischæmic zone becomes small. The centre of the injured zone dies. The maximal RS-T junction displacements now develop and with them abnormalities in QRS *as well, of which the appearance of* Q is the most signif-cant, showing a *transmural infarct* [illegible]

[illegible] healing the injured zone diminishes, for some of it recovers to the ischæmic state and some dies completely. It may now no longer be in contact with the [illegible] primarily were seen, come back and may persist.

Summary. The development of the abnormalities in the cardiogram may be based on the following fundamental phases.

INDEX

produced first the primary T wave negativity and then the *junction displacements of injury*. *Later the secondary T negativity* appeared. The ischæmia phase begins at once and lasts just over half a minute. When there is partial occlusion, release of the ligature is followed by recovery and disappearance of the negative T wave. These observations support the theoretical explanations which Bayley and others have put forward to account for the progressive changes in curves of ischæmia and of injury. It will be remembered that transient changes in T have been recorded on many occasions during an attack of angina pectoris.

REFERENCES

1 BAYLEY (1942) *Amer Heart J*, **24**, 514.
2 HILL (1946) *Amer Heart J*, **32**, 72
3 GARDBERG, ASHMAN (1943). *Arch int Med*, **72**, 210
4 SCHELLONG, HELLER, SCHWINGEL (1937) *Ztschr f Kreislaufforsch*, **29**, 497
5 WILSON, JOHNSTON (1938) *Amer Heart J*, **16**, 14
6 SCHELLONG, SCHWINGEL, HERMANN (1937) *Arch f Kreislaufforsch*, **2**, 1
7 SCHELLONG, SCHWINGEL (1937) *Ztschr f Kreislaufforsch*, **29**, 596
8 HOWARD (1946) *Amer Heart J*, **31**, 191
9 WILSON, MACLEOD, BARKER (1931) *Tr Assoc Amer Phys*, **46**, 29
10 WILSON AND OTHERS (1935) *Amer Heart J*, **10**, 46
11 ASHMAN, BYER (1943) *Amer Heart J* **25**, 16
12 ASHMAN, BYER (1943) *Amer Heart J*, **25**, 36
13 ASHMAN, GARDBERG, BYER (1943) *Amer Heart J*, **26**, 473
14 ASHMAN (1943) *Amer Heart J*, **26**, 495
15 GOLDBERGER (1942) *Amer Heart J*, **24**, 378
16 BAYLEY (1943). *Amer Heart J*, **26**, 769
17 BAYLEY, MONTE (1943) *Amer Heart J*, **25**, 262
18. BAYLEY, LA DUE (1944) *Amer Heart J*, **28**, 54